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CLINIC OF DR. HENRY MONROE MOSES

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PROBLEMS IN DIAGNOSIS

Case I. Multiple Serositis.
Case II. Raynaud's Disease, Central Nervous System Involvement.
Case III. Pneumonia of Tuberculous Origin.

EVERY patient examined by a physician or surgeon presents a problem in diagnosis. Some of these problems are more difficult of solution than others. Each one is worthy of our best efforts and consideration in its solution.

CASE I. MULTIPLE SEROSITIS

Our first patient today is a Russian laborer, fifty-five years old, who has been in this country thirty years. As you can readily see by the position of this man in bed, sitting up, leaning forward, bracing himself by holding his flexed knees, and using his accessory muscles of respiration, that he is suffering from air hunger. His breathing is rapid and shallow; his face and hands are cyanotic. This is not his first visit to the hospital, and today is the eighty-third day after his last admission. He remained at the hospital one hundred and thirty-two days on his previous visit here, after which time he was discharged, somewhat improved, at his own request and contrary to advice. Two days later he was readmitted, and his condition was much the same as you see him now. The treatment has been directed

toward diminishing the cardiac burden. His dyspnea and cyanosis are not due to any acute inflammatory disease of the lungs, to tumor of the lungs, nephritis, or diabetes mellitus.

At the time of his previous admission this patient was semi-comatose, was compelled to use the back-rest, was cyanotic, dyspneic, and had a rapid, thin, irregular pulse. Examination of his chest showed one of the emphysematous type with but little expansion on respiration, the breath sounds showed emphysema, and many moist râles at both bases. The heart sounds were weak, distant, rapid, and irregular. The apex-beat could be felt with difficulty at the sixth interspace in the midclavicular line. A systolic murmur was heard at the apex and transmitted to the left axilla. His blood-pressure was 130 systolic, 80 diastolic. The liver was enlarged and tender; it could be felt 7 cm. below the costal margin. The spleen was not palpable. There were no ascites, no abdominal tenderness except over the liver, and no abnormal masses were felt in the abdomen. There was no edema of the legs. The patient's mental condition was not clear, and a reliable history could not be obtained at the time of admission. A provisional diagnosis was made of myocardial degeneration with insufficiency, and hypertrophic liver. With rest and medical attention directed toward the cardiac insufficiency, the patient's condition improved. After two months in the hospital, he complained of pain in the left chest, with the development of signs of pleurisy on that side. Later, signs of fluid appeared in both pleural cavities. The temperature at this time varied between 99° and 100° F., and the pulse was 100 beats per minute. Thoracentesis of the left pleural cavity was performed and 950 c.c. of a clear, straw-colored fluid obtained. Fluid accumulated rapidly in both pleural sacs, and during the following two months thoracentesis was performed twelve times, fluid being obtained from both pleural sacs. No signs of pulmonary tuberculosis were present. The blood Wassermann was negative. The blood chemistry showed:

Urea,	22	mg. per 100 c.c. of blood
Creatinin,	1.2	mg. per 100 c.c. of blood
Sugar,	90	mg. per 100 c.c. of blood

The urine was normal. The chest fluids showed no organisms; no growth was obtained on culture. After one hundred and thirty-two days in the hospital the patient demanded his release and left the hospital contrary to advice. Two days later he returned as a patient, and after eighty-three days of care there is still much discomfort present. A moderate amount of fluid was present in the peritoneal cavity at the time of his readmission; fluid was present also in both pleural sacs, and there was a slight edema of the ankles. Thoracentesis has been performed six times during this admission to the hospital, making eighteen operations to date. His temperature at this time is 102.2° F., his pulse 90 beats per minute, and his respirations 28 per minute. There is evidence of a pericarditis with a moderate amount of fluid in the pericardial sac. The patient is becoming progressively weaker, and the prognosis is bad. At the present time there is but a small amount of fluid in the pleural sacs, although the patient begs us to aspirate because of the difficulty in breathing. This discomfort is due, no doubt, to the pleura becoming thickened and adherent. His laboratory findings correspond to those of his previous admission, with the exception that at this time there is an increase in the number of leukocytes. The blood-picture is as follows:

4,896,000 red blood-cells
14,600 white blood-cells
70 per cent. polymorphonuclear cells
25 per cent. small mononuclear cells
3 per cent. large mononuclear cells
2 per cent. transitional cells
90 per cent. hemoglobin

The question arises with this patient as to whether we have fluid in the serous sacs because of a failing heart and incompetence of portal circulation, or have we a patient with multiple serositis, or polyserositis, as we understand the condition.

Evans[1] states that chronic perihepatitis, associated with varying degrees of chronic inflammation of the pericardium and pleuræ, as a local manifestation of diffuse chronic peritonitis has been recognized for more than half a century. Rolleston re-

stricts the name multiple serositis to this condition, and includes in this category the chronic hyperplastic perihepatitis described by Curschmann in 1884, and called by him Zuckergussleber, sugar-iced liver. In 1842, Rokitansky,[2] the great Bohemian pathologic anatomist, described the postmortem examination of a patient who had died from asthenia. There was found chronic inflammation and partial obliteration of the great serous sacs in the thoracic and abdominal cavities, almost complete obliteration of the pericardial sac, the result of an antecedent pleuritis and pericarditis. Because of the chronic hypertrophic peritonitis, the liver and the spleen had become encased in adhesions, and the small intestines were locked together, although they were not locally obstructed. In regard to peritoneal involvement, Mayo[3] writes, "Multiple serositis is a poor term for this syndrome, which probably does not represent a definite disease, but rather a manifestation of chronic inflammation of three contiguous serous sacs—the pericardium, the pleuræ, and the peritoneum—the result of many causes which we have heretofore recognized only in the terminal stage. The condition is, indeed, surgically interesting when found upon abdominal incision."

In 1896 Pick[4] described under the term "pericarditic pseudoliver cirrhosis" three patients whose ailment was predominantly ascites of long duration, together with enlarged liver, but at autopsy, in each instance, showed thickened and obliterated pericardium not suspected during life. All of these cases presented marked perihepatitis. This communication became the subject of much discussion at the time, and the condition described has been called Pick's disease, although it was known to earlier writers.

A thorough review of the condition was published by Kelly[5] in 1903, who states, in the majority of cases when chronic adhesive or obliterative pericarditis gives rise to symptoms, the symptoms that arise are those of failing cardiac compensation—palpitation of the heart, dyspnea, cyanosis, cough, generalized edema, effusions into the several serous cavities of the body, with venous congestion of the organs. On the contrary, in the cases that simulate cirrhosis of the liver clinically, the first

symptoms are sensations of fulness, oppression and weight in the upper abdomen, or there may be apparently a sudden onset with acute pain. Ascites may be prominent. In these cases a diagnosis of cirrhosis of the liver is usually made. The symptoms of the disease vary according to the serous cavity which is most extensively involved. The feature possessed by cases in common, as reported by Kelly, is wide-spread disease of the serous membranes, and the most common lesion is chronic hyperplastic serositis. The cause of multiple serositis is obscure. Tuberculosis and syphilis must be excluded.

This condition is known in Italy as Concato's disease, and in France as perivisceritis.

Our patient presents many of the features of multiple serositis: the cardiac embarrassment, the enlarged, tender liver, the fluid in the serous sacs, and the rapid formation and accumulation of fluid in the pleural sacs after removal. The laboratory reports all of these fluids removed from the pleural sacs as transudates and not exudates. Our final conclusion is that this patient is suffering from multiple serositis.

CASE II. RAYNAUD'S DISEASE, CENTRAL NERVOUS SYSTEM INVOLVEMENT

Our second patient presents a different picture than the one we have been considering. This man, thirty-six years old, was admitted to Kings County Hospital ten days ago from another hospital, where he had been a patient for seven weeks. As you can see, he is an adult white male, lying on his back with his knees flexed; he is emaciated, looks chronically ill, and is in pain. Examination of his head, from which the hair has been shaved, shows the upper margins of the ears to be gangrenous; over the molar bones, the tip of the nose, and upon the upper lip below the nose are spots which are gangrenous. Inside of his mouth, the soft palate, the uvula, and the tonsillar pillars are discolored and gangrenous. Examination of his body shows multiple extensive gangrenous areas, which are superficial and do not invade the deep tissues; these areas are on his shoulders, arms, forearms, hands, fingers, hips, thighs, knees, legs, toes, and

scrotum. The little finger of the right hand is black and gangrenous; his knees, legs, and toes are extensively involved. His

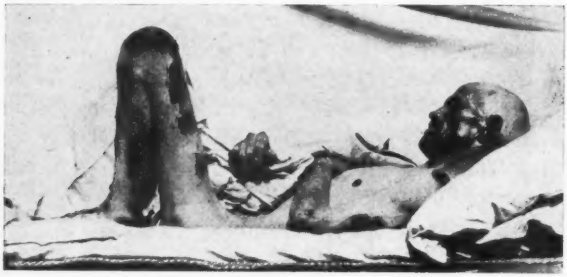

Fig. 123.—Showing left side of patient with extent of the involvement of the tissues.

trunk, anteriorly and posteriorly, is not involved, and the flexor surfaces are comparatively free from lesions. Photographs (Figs. 123–130) which have been taken show clearly the extent,

Fig. 124.—Showing the involvement of the right ear and right cheek.

character, and symmetry of the involvement. The patient is intelligent and rational, and gives the following history: By occupation he is a belt-maker, and the question arises naturally

as to whether or not his occupation is responsible for this condition. This aspect of the history has been reviewed thoroughly

Fig. 125.—Showing the involvement of the left ear and left cheek.

by Dr. Gaetano de Yoanna, of the surgical service, who has information not only from this patient's place of business but also from other factories where the same materials are con-

Fig. 126.—Showing the involvement of the right ear, right cheek, right shoulder, right forearm and hand, also the gangrene of the fifth finger.

stantly used, and the conclusion is that the man's occupation is in no way responsible for his condition.

Four and one-half months ago, or about the middle of April, upon returning home one cold rainy evening, the patient noticed

that the tips of his ears were blue. There was no pain with this discoloration. Having been exposed to the rain and chilly wind,

Fig. 127.—Showing the involvement of the right forearm and hand, also the involvement of the right hip, knee, leg, and foot.

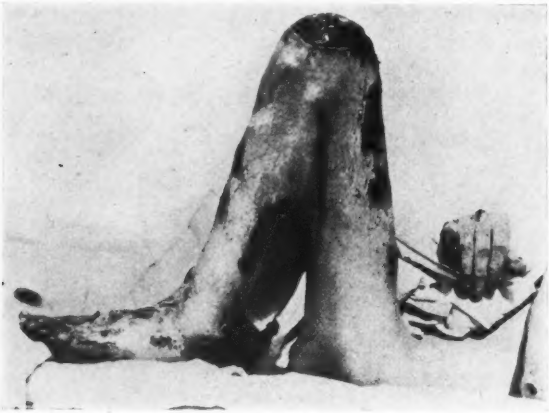

Fig. 128.—Showing gangrene of the right fifth finger, also the extent of the involvement of the left thigh, knee, leg, and foot.

he felt that this was the cause of the condition. The discoloration remained a few days and then disappeared, to return again

upon re-exposure to cold. A local physician was called in and told the patient that his ears had been frost-bitten, although April cold is not severe, and there was no history of previously

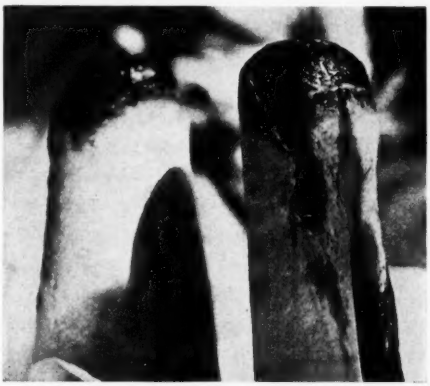

Fig. 129.—Showing the extent of the involvement of both knees.

Fig. 130.—Showing the involvement of both feet.

freezing the ears. This physician prescribed an ointment for local use; the patient obtained no relief under treatment. One month later he noticed a discoloration appearing on the fingers

and extending to the hands. Two weeks later the discoloration of the ears and the hands became permanent. On June 16th, the evening prior to his admission to the hospital from which he was sent to Kings County Hospital, upon removing his shoes and stockings, the patient noticed that his feet and legs as high as the knees were blue, cold to the touch, slightly swollen, but not painful. His mother, an intelligent German woman, said that they looked as though he were wearing a pair of boots. Up to this time this man had been attending to his work daily, but with this new development of discoloration appearing on his feet and legs, he felt it necessary to enter a hospital for treatment. The discolored patches on his face appeared the first day he was a patient in the hospital. His family history is good, his mother, father, one sister, and three brothers are alive and well, and there is no history of any sisters or brothers dead. No tuberculosis nor cancer have been present in the family. His previous personal history shows that he had the simpler diseases of childhood, with good recoveries. He had an attack of tonsillitis eight years ago, with three weeks' illness, and a good recovery, with no recurrence. He has never had rheumatism, diphtheria, scarlet fever, pneumonia, malaria, typhoid fever, or influenza. During his stay at the first hospital these areas have become more extensive and gangrenous in spite of local care and supportive treatment. He was transferred to the Kings County Hospital with a diagnosis of Raynaud's disease, after seven weeks' treatment. Figures 123–130 show the extent of the lesions upon his admission here. He has been treated under the co-operative care of the medical, surgical, pathological, neurological, and dermatological services. He shows the effects of absorption of toxic material; his temperature varies between 100° and 102° F., his pulse has been between 100 and 120 beats per minute; his respirations are from 16 to 18 per minute. His urine is normal for his condition, and does not show the presence of kidney disease. His blood chemistry is as follows:

Urea,	23	mg. per 100 c.c. of blood
Creatinin,	1.2	mg. per 100 c.c. of blood
Sugar,	85	mg. per 100 c.c. of blood

His blood-count shows:

4,128,000 red blood-cells
16,300 white blood-cells
86 per cent. polymorphonuclear cells
10 per cent. small mononuclear cells.
3 per cent. large mononuclear cells
1 per cent. transitional cells
80 per cent. hemoglobin

The blood Wassermann is negative. The sputum is negative for the tubercle bacillus. As you can see, this man is seriously ill. The ulcerations although extensive are not deep, and there is little destruction of tissue other than the superficial tissue. A biopsy specimen has been ordered from one of these areas, but the laboratory report has not yet been returned. However, there is a large enough extent of surface for the absorption of much toxic material. Pain is present, and the patient has flexed his knees so as to be in the most comfortable position.

The severity of the condition, the fact that this is his first attack of this nature, the patient's usual good health, the symmetry and extent of the involved areas cause us to feel that this condition is more than our concept of the syndrome called Raynaud's disease, and a number of additional diagnoses have been suggested. Everyone who has examined this patient feels that there must be present some lesion of the central nervous system.

One of the diagnoses suggested was multiple gangrene in adults, as described by Stelwagon and Gaskill,[6] who state that the term is employed to include manifestations of cutaneous gangrene not dependent upon an underlying diabetes, and which has been described under the name of spontaneous gangrene of the skin, disseminated gangrene, hysteric gangrene, gangrenous zoster, and dermatitis gangrenosa. The lesions may be few or numerous, and begin with an erythematous spot, erythema gangrenosum, which soon becomes gangrenous without any intermediate stage, or there may be slight vesiculation, or serous exudation under the epiderm. Cases in men are

rare, but have been reported. The causes are doubtless varied, but a fair presumption is that two factors are necessary: a weakened resisting power in the skin due to a general neurosis, or trophoneurotic disturbance, or blood-vessel changes, and a local infective agent. The condition in this patient is not an erythema, as it is not inflammatory in origin. The diagnosis of diffuse idiopathic atrophy of the skin has been suggested. Another suggestion is toxic erythema multiforme bullosum. In regard to this possibility, Dr. William H. Best, attending physician on the dermatological service, comments as follows: "This is not toxic erythema multiforme bullosum, as erythema multiforme bullosum is an inflammatory dermatitis, the lesions starting as an inflammation and subsequently becoming a bleb. The disease being toxic, there is no regularity of distribution, although in mild cases there is a predilection for the extensor surfaces. In erythema multiforme bullosum the mucous membranes are usually involved, and I have never seen gangrene following the lesions. In this patient the lesion starts from an apparently normal integument. There is a rather rapid exudation of serum and blood from the capillaries and arterioles into the derma. This would indicate a tophic nerve disturbance, and the same trophic nerve disturbance causing subsequent starvation of the part, gangrene supervenes. Considering the symmetry of the lesions, it would seem that the lesions are the result of a central nervous system pathologic condition. His present toxic condition is simply due to toxic absorption from gangrenous areas. His general health was good up to and after the beginning of this illness. For this reason, multiple gangrene in adults can be ruled out. While this patient does not present the typical clinical picture of Raynaud's disease, as we are accustomed to see it, yet the entire symptom complex types up nearer this disease than any other I can think of. However, I am of the opinion that the cutaneous condition is the result of central nervous system involvement rather than any systemic toxemia."

The history of this patient recalls that of a patient admitted to Kings County Hospital a few years ago, whose skin condition was not unlike that of the patient we have just seen.

An eight-year-old boy was admitted December 7th, with the following history: Three weeks before admission the patient began to cough, and invariably vomited after each coughing spell. He had an average of two attacks per hour. During this time he complained of slight abdominal pain. Two weeks before admission he complained of cramps in his feet, and when his shoes were removed his feet were found to be swollen. The following day they became cyanotic. A physician, called in by the parents, made a diagnosis of rheumatism. Severe itching of the ears appeared on this day, to be followed rapidly by itching of the nose, face, fingers, and various parts of the body. The pain in the feet continued. Three days later the boy had a convulsion and remained in a stupor for several hours. The next day his ears became discolored around the margins, and several joints became swollen. The boy's father stated that he had attacks of dyspnea since his illness. The patient's past history was good, except for one incident. Several weeks before admission to the hospital he had a discharge from the ear following a "cold in the head." His family history was good. During his stay in the hospital the patient had definite signs of bronchopneumonia. No cardiac pathology was noted. Areas of gangrene developed in the ears, over the acromial areas, the olecranon processes, the feet, the fingers, and toes. The laboratory tests gave no definite information. The temperature remained about 102° F., and the patient died on the ninth day in the hospital. Permission to perform a postmortem was obtained, and the findings briefly summarized by Dr. William W. Hala, in charge of the pathologic service at the Kings County Hospital, are as follows: This patient showed the following lesions on postmortem examination. The body was emaciated, the helices of both ears had sloughed off as a result of gangrene. There were gangrenous areas in the following portions of the body: around both nostrils, the lower lip and left angle of the mouth, a circular punched-out area exposing the right acromion, gangrenous ulcerations exposing both olecranon processes, a circumscribed round area of gangrene on the flexor side of the left forearm near the wrist, a purplish bullous area on the inner surface of

the middle third of the right forearm, the proximal pharyngeal joints were exposed by sloughing of the tissue. An irregular oval area of necrosis was observed over the first lumbar vertebra, and a similar larger area was present over the sacrum. There were gangrenous areas over both trochanters and four symmetrically placed gangrenous areas, averaging from 4 cm. in diameter, in the vicinity of the superior angles of the iliac bones, anteriorly and posteriorly. Both feet showed gangrenous areas, the parts involved being the heels, the instep, big toe, and all other toes of the left foot, also the big toe and distal phalanges of the right foot. Wherever noted, the gangrene was of the dry type and sharply demarcated. The gross anatomic findings in this case were:

Acute vegetative mitral endocarditis
Acute myocarditis
Confluent lobular pneumonia
Infarction of the spleen
Acute nephrosis
Multiple gangrenous dermatitis

The summary of the histopathologic findings were:

Cloudy swelling of the myocardium
Subacute bacterial endocarditis
Acute exudative mediastinal lymphadenitis
Confluent lobular pneumonia
Acute septic infarction of the spleen
Bacterial thrombosis of the splenic artery
Cloudy swelling of the liver
Acute nephrosis
Gangrenous dermatitis, secondary to septic (bacterial) thrombosis of the terminal superficial capillaries

The organism in question was a streptococcus, and the terminal capillaries were entirely occluded by these cocci.

Comment.—This is an unusual case of multiple gangrenous dermatitis, secondary to septic thrombosis of the capillaries, with the primary focus in the mitral valve. The cardiac condition was not suspected or diagnosed during life.

The time at our disposal will not allow us to speculate comparatively upon these two cases.

CASE III. PNEUMONIA OF TUBERCULOUS ORIGIN

Our third patient today is this sixteen-year-old negro boy who was admitted to the hospital two weeks ago. This boy had been attending summer school a half-day, and working the other half, apparently in good health. Three weeks before admission, or five weeks ago, he noticed that he was drowsy and "dopey," as he expressed it. He felt weak and went to bed because of weakness and that tired feeling; there was some fever present. One week later he started to cough and expectorated a white frothy liquid. There were no hemoptysis, no epistaxis, no headache, no nausea, no vomitting, no dizziness, and no pain in the chest. He had been in bed three weeks before admission to the Kings County Hospital. His chief complaints were:

Cough
Expectoration
Weakness
Fever

Except for increased emaciation, his general appearance on admission was much as you see him now, lying on his back, his eyes shut, his mental processes slow, and irrational at times. On admission his temperature was 102.2° F., his pulse 90 beats per minute, his respirations 24 per minute. He appeared acutely ill.

The history obtained from his mother was that the boy had frequent colds, with no loss of weight during the past three years. His appetite had always been good, and until this recent illness his health also had always been good. His physical examination reveals a fairly well-developed and nourished negro lad, sixteen years old, drowsy, with slow mental processes, who shuts his eyes and goes to sleep if permitted to do so. Upon admission he was rational in his conversation and his answers. His tongue is dry, coated, and there are sordes on his teeth and lips. His breath is foul. The chest is well developed, the respirations are shallow, increased in number, with the expansion diminished on the right side of the chest. Resonance is diminished, also, at the right apex and axilla. Tactile and vocal

fremitus are increased over both upper lobes. There are many coarse and fine moist râles, as well as many sonorous râles heard throughout both upper lobes, more marked anteriorly. There are no true bronchial breath sounds, but there are areas of bronchovesicular breathing over the upper lobe anteriorly near the edge of the sternum on the right side. There are many fine crepitant râles at the right base, and fewer fine crepitant râles at the left base extending to the left axilla. The heart sounds are rapid, regular, of fair quality, and no murmurs are heard. The following day bronchial breathing was evident over both upper lobes, and many dry and moist râles of all sizes could be heard throughout the entire chest. In the absence of any laboratory findings, what condition is present in this patient? There is no doubt that he is having some form of severe pulmonary upset, a diffuse pneumonitis with localized consolidation in the upper lobes. What may be the cause of this disturbance? In addition to the pneumonia, is the patient suffering from some other serious condition? Are we able to exclude encephalitis lethargica, typhoid fever, miliary tuberculosis, which is not uncommon among the negroes, or a severe, rapid form of pulmonary tuberculosis with a general tuberculous toxemia. A provisional diagnosis of bronchopneumonia of tuberculous origin was made at the time of his admission. The results of the laboratory examinations follow; the blood-count was:

5,312,000 red blood-cells
7,500 white blood-cells
72 per cent. polymorphonuclear cells
10 per cent. small mononuclear cells
12 per cent. large mononuclear cells
3 per cent. transitional cells
3 per cent. eosinophils

His blood chemistry showed:

Urea,	20	mg. per 100 c.c. of blood
Creatinin,	1.2	mg. per 100 c.c. of blood
Sugar,	106	mg. per 100 c.c. of blood

The blood-culture was sterile.

The urine was of a specific gravity of 1018—it had a trace of albumen and no casts.

The Widal reaction was negative for typhoid fever.

The blood Wassermann was negative for syphilis.

The spinal fluid Wassermann was negative for syphilis. The sputum was negative for the tubercle bacillus.

The sputum showed no reaction to type for the pneumococcus.

The roentgen-ray examination of the chest showed "a consolidation of both upper lobes, that of the right upper lobe apparently undergoing resolution." From a second picture, taken two days ago, "the pulmonary condition remains practically the same as in the first picture."

Daily examinations of the sputum for the tubercle bacillus were negative until two days ago, when the tubercle was present in the specimen.

A second blood-picture made one week ago shows the changes in the blood consistent with the disease, and shows the effect and progress of the condition; the findings are:

4,320,000 red blood-cells
9,900 white blood-cells
60 per cent. polymorphonuclear cells
35 per cent. small mononuclear cells
2 per cent. large mononuclear cells
3 per cent. transitional cells
80 per cent. hemoglobin

A second spinal fluid examination showed a normal spinal fluid.

This patient remained drowsy, and on the sixth day became slightly irrational due to toxins. His condition has become progressively worse, until he is as you see him, emaciated and irrational. The prognosis is bad.

In following the course of the disease in this boy it is not difficult to exclude some of the conditions mentioned above. Examination of his chest today, as you can hear, still shows consolidation of both upper lobes, and we can hear, easily, râles of all types throughout the lungs. There are no evidences of peritoneal or intestinal tuberculosis. The boy is dying of an acute outbreak of pulmonary tuberculosis, causing consolida-

tion of both upper lobes, together with a generalized tuberculous toxemia. The course of his temperature, pulse, and respiration is shown in Fig. 131.

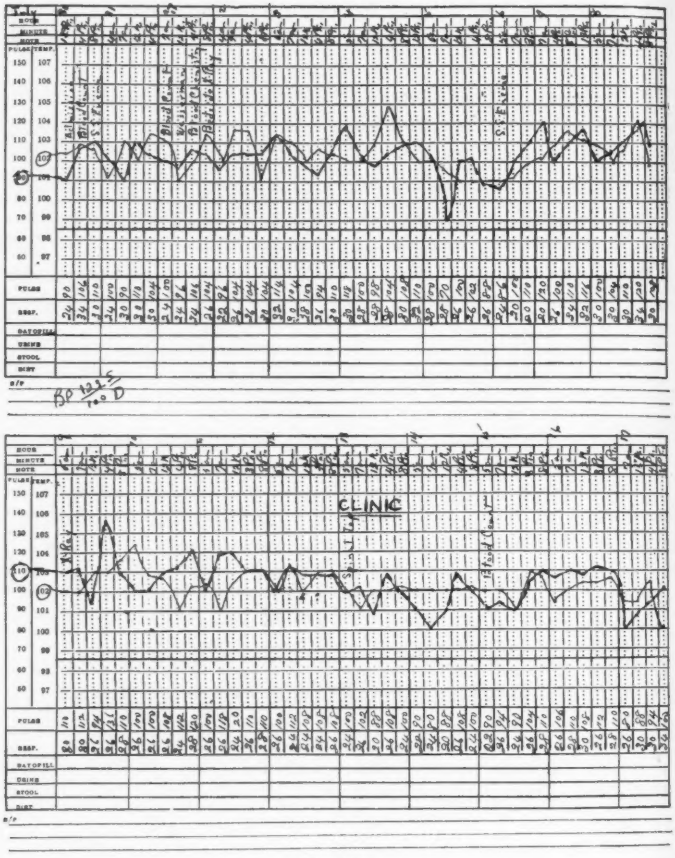

Fig. 131.

The admission to the hospital of any patient with pneumonia presents an interesting and instructive problem whatever the etiologic factor causing the consolidation may be. In a review of a series of 2450 patients on this service, over a period of

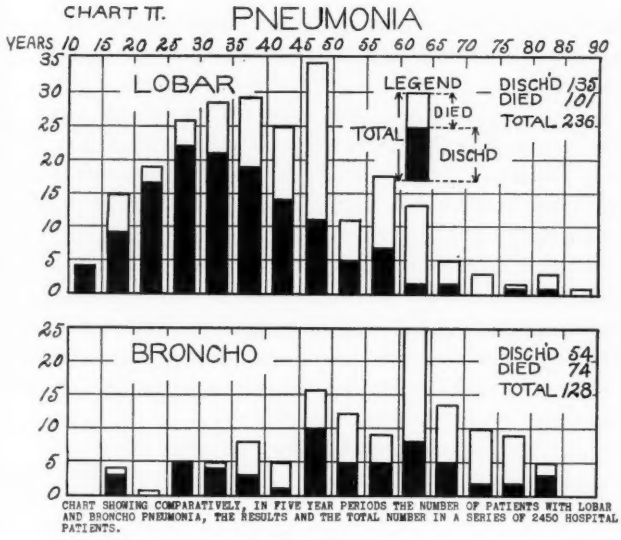

CHART SHOWING COMPARATIVELY, IN FIVE YEAR PERIODS THE NUMBER OF PATIENTS WITH LOBAR AND BRONCHO PNEUMONIA, THE RESULTS AND THE TOTAL NUMBER IN A SERIES OF 2450 HOSPITAL PATIENTS.

Fig. 132.

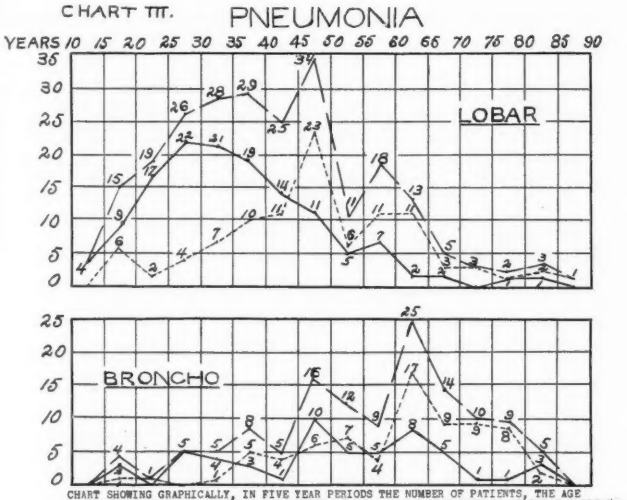

CHART SHOWING GRAPHICALLY, IN FIVE YEAR PERIODS THE NUMBER OF PATIENTS, THE AGE INCIDENCE OF THE DISEASE, THE TYPE OF PNEUMONIA AND THE DISPOSITION OF THESE PATIENTS.

Fig. 133.

three and one-half years,[7] it is of interest to note that there were 364 patients having pneumonia. We may see from Fig. 132 the number of patients who recovered, and the number who died, compared to the total number of patients with pneumonia. This comparison is shown graphically in Fig. 133. Among these patients with pneumonia, 8 were in advanced stages of pulmonary tuberculosis. Six of the 8 patients died during the acute attack.

A study of the three patients who appeared before us today suggests many important questions in diagnosis; when we realize that at any time in our private practice or in our hospital work conditions such as these, which we have reviewed, may arise, we find a stimulus for greater efforts in our care of patients.

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CLINIC OF DR. HENRY JOACHIM

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TWO CASES OF ASCITES

Case I.—The first case presented is that of a male, aged fifty-seven, married, and a presser by occupation. He was first admitted to the Long Island College Hospital in May, 1924, with the complaint of abdominal distention and swelling of the feet. His present and fifth admission dates from September 26, 1927. He sought admission to the hospital on account of progressive swelling of the abdomen and feet, and increasing dyspnea, cough, and cyanosis.

The previous history of the patient revealed an excessive indulgence in beer to the extent of a pint and a half for about thirty years, with the addition of two or three glasses of brandy daily, for a similar period. He averaged about twenty cigarettes daily with an occasional cigar. Venereal infection was denied. About twenty-eight years ago his appendix was removed. The patient states that he has had a chronic cough for about thirty years and that he is subject to attacks of bronchitis and asthma.

The present illness began about in May, 1923, when the patient experienced some pain in the upper abdomen, which seemed to have no relation to his food, but was aggravated by exertion. He was admitted to a hospital in October, 1923, where, after rest and medication, he was discharged at the end of four weeks greatly improved. He was told at that time that "his liver was swollen." In the early part of 1924 his pain recurred, his abdomen began to enlarge, and his feet began to swell. He entered the Long Island College Hospital, and at the end of two weeks was so much improved that he was ready for discharge. In March, 1925 the patient was again admitted

with a repetition of his symptoms, but in an aggravated form. About 3600 c.c. of fluid were removed from his abdomen, and in eighteen days he again left the hospital and returned to his occupation. In December, 1926 he again returned with the previous symptoms, but with marked dyspnea and cyanosis. At the end of two weeks with restriction of his fluid intake and salt-free diet, with digitalization, his edema and dyspnea disappeared, he was discharged and returned to his work for two months against advice. He was re-admitted in May, 1927, and remained for three weeks. With digitalis, ammonium chlorid, and salyrgan he again improved. He continued at his occupation for two months, when all his symptoms returned in a much severer form, and he entered the hospital on September 26, 1927.

His physical examination on that date was reported as follows: Marked cyanosis and orthopnea, facial capillaries prominent, chest barrel shaped, with poor respiratory excursions. Veins at the side of the chest prominent and fill from below upward. Tactile fremitus is diminished throughout, and the percussion note at the right base is somewhat dulled. There are sibilant and subcrepitant râles at both pulmonary bases. The apex-beat is in the fourth interspace in the midclavicular line. The maximum cardiac dulness measured 19 cm., and the right heart was percussed about 6 cm. from the midsternal line. The aorta measured 6 cm. A 2-meter chest plate confirmed these cardiac measurements. Absolute cardiac dulness was obliterated, and the sounds at the apex were distant and absent at the base. At the apex there was a systolic blow transmitted toward the liver (tricuspid insufficiency?). The pulse-rate was 90 and regular. The abdomen was markedly distended and the umbilicus protruded. The abdominal veins were not prominent. Free fluid was demonstrated by the usual physical signs. The liver was palpable by dipping displacement palpation. The maximum liver dulness in the midaxillary line measured 18 cm. The spleen was not palpable. The extremities were edematous and cyanotic. Knee-jerks were present. The blood findings were negative for morphology, serology,

and chemistry. Urine examination revealed no evidences of renal pathology. The blood-pressure was 112/68.

Summary.—The patient had a history of a cough of about thirty-five years' duration, excessive indulgence in alcohol, and in the past four years frequent attacks of abdominal distention, epigastric pain, edema, dyspnea, and cyanosis. His heart, particularly the right, was enlarged, as was the liver. We felt that in this case his symptoms were primarily cardiac, and produced by an emphysema and chronic bronchitis acting on the right heart (cor pulmonalis). His liver probably was fatty and cirrhotic from cardiac stasis and alcohol and was partly responsible for his ascites and abdominal pain. The rapid response to cardiac therapy strengthened our assumption. The free intervals between attacks have become progressively lessened and the severity of his symptoms with each attack is increased, evidences that his cardiac reserve is becoming less efficient.

Case II.—Male, fifty-three, presser, was admitted on September 9, 1927, with the complaint of enlargement of the abdomen and loss of weight. At the age of eighteen the patient had a malarial attack of two weeks' duration, which responded to therapy and which was not followed by recurrences. At thirty-five he had pneumonia, and at the age of forty-three suffered from a carbuncle of the left toe, which lasted for about six months and finally yielded to incision and drainage. His venereal and alcoholic history is negative.

The present history began in March, 1927, when the patient noticed that his face and arms began to become thinner, and that he was weak. At that time he also noticed some puffiness of his feet. His abdomen began to enlarge and he consulted a physician, who concluded that the patient had some fluid in his abdomen and suggested hospitalization. He entered a hospital on June 15th, where his abdomen was tapped and a large amount of clear fluid was removed. In ten days there was a re-accumulation of the fluid and operation was suggested to him. On June 25th an exploratory operation was performed, and the operative findings were reported as follows: free fluid in the abdomen,

the liver small and hobnailed, spleen not enlarged. A Talma-Morison operation was performed. He remained in the hospital for eight weeks, during which time his abdomen was tapped on three occasions. A ventral hernia developed at the site of the operative scar and the abdomen refilled. He was admitted to the Long Island College Hospital on September 9th. The patient had no other complaint except abdominal distention. His physical condition was reported as follows: Weight, 140 pounds, height, 66 inches, face and extremities emaciated. The tongue was beefy, the pharynx congested, and the tonsils cryptic. The radial arteries were slightly fibrotic. The superficial veins at the side of the abdomen, back, and loins were prominent. The abdomen was markedly distended and free fluid was demonstrated. The liver dulness measured 8 cm. in the midaxillary line. Ventral and bilateral inguinal hernias were present. Slight pretibial edema was present. An abdominal tap was undertaken and 7320 c.c. of dark fluid were removed. The patient was given ammonium chlorid, theocin, and salyrgan intravenously, with temporary increase in the diuresis. One week later 7100 c.c. of fluid were removed. In about ten days the patient's weight increased 12 pounds and his distention became extreme, so that it was necessary to repeat the paracentesis by the withdrawal of 9000 c.c. The average gravity of the ascitic fluid was 1010—on two occasions blood was present. There were no increased values in his blood chemistry or icteric index. The Wassermann reaction was negative. The urine showed a low fixed gravity of 1006 to 1009, but was otherwise negative.

We considered this case to be one of cirrhosis of the liver, which was substantiated by the operative findings. Some uncertainty exists as to the cause of the cirrhosis, since alcohol, syphilis, and vascular stasis can be excluded. An unusual feature is the absence of the enlargement of the spleen and visible portocaval venous anastomoses. The absence or insufficient development of the latter is probably accountable for the rapid accumulation of the ascitic fluid.

The chief complaint of the two patients presented was abdominal distention and fulness. A fluid collection in the ab-

domen should always be suspected in any patient whose history reveals an abdominal enlargement, and a gain in weight with a diminution of the urinary output. Ascites is usually present with generalized edema.

Enlargement of the abdomen is usually due to four general causes:

1. Obesity with a deposition of omental fat (omental lipoma).
2. Accumulation of gas in the intestinal tract (meteorism, tympanites) or free in the peritoneal cavity (pneumoperitoneum).
3. Pregnancy, tumors, cysts, hydronephrosis, or a distended bladder.
4. Fluid in the peritoneal cavity (ascites, hydroperitoneum).

Any or all of these combinations may present themselves.

The physical signs of ascites are usually not difficult to demonstrate. If, however, the amount of fluid is small (less than 2000 c.c., as determined experimentally on the cadaver by Fr. Müller), if the abdominal walls are thick, edematous, or rigid (peritonitis, meningitis), or if the fluid is viscid or encapsulated by adhesions, considerable difficulty may be experienced. Tympanites may precede the ascites and obscure the latter. Portal has aptly likened this preascitic tympanites to "the wind before the rain."

The abdomen is usually prominent, and with fluid collections with good abdominal musculature it assumes a globular or spherical outline. In the early stages the muscles are tense from irritation of the peritoneum, but later flaccidity develops. If the abdomen is flaccid and a diastasis of the recti is present, there may be a distinct bulging in the midline (conical abdomen) with a filling out of the lateral abdominal walls in the dorsal decubitus (frog belly). The umbilicus may be prominent, especially in the presence of a hernia. In carcinoma of the peritoneum it has occasionally been possible to palpate nodules through hernial openings. In ascites of tuberculous origin the umbilicus may be reddened and indurated (omphalitis), and in carcinoma of the peritoneum retracted and nodular. In hemoperitoneum (ectopic rupture) the umbilicus has a bluish discoloration (Cullen sign). In the presence of free bile in the peritoneum (chole-

peritoneum) there is occasionally a yellow discoloration (Ransohoff sign). With obesity and abdominal edema the umbilicus may be obliterated or buried.

With excessive distention the linea albicantes may be prominent, and in portal or caval stasis prominent venous anastomoses may be observed. Ascites occurring in males with absent abdominal or axillary hairs, or in females with the inverse type of pubic hair, suggests hepatic cirrhosis (Chvostek's habitus). Ascites in brunettes with red beards or axillary hairs points to a tuberculous peritonitis (dysharmony of Schmidt). With a patent funicular process (testicular, infantile hernia), small amounts of ascitic fluid may gravitate into the scrotum when the patient stands and be mistaken for a hydrocele. On assuming a recumbent posture the fluid recedes into the abdominal cavity.

Fluid percussion waves can usually be demonstrated, except in cases where the fluid is under extreme tension or when the abdominal walls are edematous. Small amounts of fluid can sometimes be recognized by the insertion of the index-finger into the inguinal canal of the patient in the standing posture, and tapping the lower abdomen when a percussion wave is perceived by the invaginated finger. In females a similar impulse is detected in Douglas's pouch. In marked ascites the uterus is depressed and the cervix is easily palpated, and in extreme cases a prolapse of the uterus occurs. Rectal examination may reveal a nodule in the rectovesical pouch in cases of carcinoma of the peritoneum (Blumer shelf). In executing the maneuver known as dipping or displacement palpation over an enlarged liver or spleen, a characteristic sensation is imparted to the palpating hand which is pathognomic for fluid in the peritoneum. Under ordinary circumstances a succussion splash cannot be elicited unless there is air in the peritoneal cavity or distention of the stomach and intestines with gaseous and fluid contents. Shifting dulness in the flanks is present, provided the fluid is not encapsulated or caused by a retroperitoneal neoplasm. In shifting the patient from the dorsal to the lateral posture the examiner must allow enough time to elapse for the gravitation

of the fluid. Tympany about the umbilicus is usually present, except in tuberculous peritonitis with a retracted mesentery, when the intestines are bound down by the shrunken mesentery and cannot float on the ascitic fluid. Tuberculous peritonitis sometimes gives a tympanitic area in the right upper abdominal quadrant and a dull percussion note in the left lower quadrant. This has been alluded to as Thomayer's phenomenon. There may be a tympanitic note in the flanks when a dilated colon is adherent to the posterior abdominal parietes. Retroperitoneal neoplasm and gravitation edemas may produce a fixed dulness in the loin. The upper level of the fluid dulness in the standing posture is usually a horizontal line which approaches the symphysis when the patient reclines. Cysts, pregnancy, and a distended bladder give a fixed line with an upward convexity.

When uncertainty exists as to the presence of fluid it can sometimes be demonstrated by percussing the umbilical region in the knee-chest position. Errors must be avoided in cases of megalocolon (Hirschsprung's disease), after the administration of a cathartic which produces fluid contents of the bowels, and in cases of pyloric obstruction with marked gastriectasis. These conditions are usually accompanied by a succussion splash. Atypical percussion findings occur in the scaphoid abdomen and collapsed intestines of meningitis complicating a tuberculous ascites. In these cases there is an absent tympanitic note throughout the abdomen. Bizarre percussion findings are present in the encapsulated ascites (serocele, hydrops, saccatus) and in echinococcus of the peritoneum. The latter is said to give alternate areas of dulness and tympany (checker-board phenomenon).

Auscultation of the abdomen may reveal bruits over the distended veins in portal or caval obstruction. The cardiac and respiratory sounds may be transmitted. The direction of the blood-current can be ascertained by the compression of the vein on either side of the stethoscope and noting the side on which the bruit disappears. The flow of blood may be toward the liver in caval or portal-vein obstruction (hepatopetal) and away from the liver in cirrhosis (hepatofugal).

Before definitely concluding the presence of ascites one must take the following conditions under diagnostic consideration:

1. Pregnancy with hydramnios.
2. Cysts of the ovary or parovarium. These present the greatest difficulty in differentiation, since ascites may complicate a cyst, particularly in papillomatous cysts when peritoneal implantation metastases occur. With torsion or rupture of a cyst there is free abdominal fluid. Gas-containing ovarian cysts make the differentiation even more difficult.
3. A distended or ruptured bladder, cysts of the urachus, or abdominal wall. With large amounts of ascitic fluid bladder symptoms may be prominent from diminished capacity due to compression.
4. Pancreatic cysts.
5. Hydronephrosis.
6. Retroperitoneal cysts or tumors. These are often accompanied by ascites.
7. Gastriectasis.
8. Omental and mesenteric cysts or torsion of the omentum.
9. Fibroids complicated by ascites.
10. Phantom tumors and hysterical pneumatosis.
11. A distended gall-bladder has been mistaken for ascites. When it has been satisfactorily established that fluid is present in the abdominal cavity, the cause and nature must be ascertained. A diagnostic tap can be undertaken. There are six general causes for fluid in the abdominal cavity:

I. Trauma.
II. Stasis of cardiac, pulmonary, hepatic, or lymphatic origin.
III. Inflammation of the peritoneum.
IV. Cachexia, hydremia, and anemia.
V. Neoplasm.
VI. Idiophatic.

I. Trauma. Incomplete postoperative hemostasis, after injury to the liver, spleen, intestinal tract, pancreas, or blood-vessels, or from the rupture of an ectopic gestation, cyst of a

Graafian follicle or corpus luteum, or rupture of a pregnant uterus, urinary bladder, or ovarian cyst.

II. Stasis. Various forms of hepatic cirrhosis, such as occur from alcohol, cardiac stasis, malaria, syphilis, Banti's disease, kala-azar, Wilson's disease, and bronze diabetes, from compression, adhesions and thrombosis of the hepatic veins (Craven Moore syndrome), mediastinitis and pericardial adhesions (Pick's syndrome), and the stasis from emphysema and chronic pulmonary disease produces ascites. Compressions, adhesions, or thrombosis of the portal vein or its tributaries produce the greatest amount of ascites with rapid accumulation after paracentesis. Portal and hepatic stasis can usually be recognized by the establishment of a collateral portocaval venous anastomosis. With obstruction of the inferior vena cava, ascites with venous anastomoses may result. Compression of the cava may result from excessive amounts of ascitic fluid. Lymphatic stasis from obstruction of the thoracic duct (filariasis, malignancy) produces a chylous fluid.

When the portal circulation is interfered with it is necessary to recognize the venous anastomoses with the caval system. These have an important bearing on the symptoms, course, prognosis, and complications. When these are well developed, there is a tendency toward rupture and toxemia from direct intestinal absorption. The various paths of communication are as follows:

1. The splenic vein communicates with the venæ coronariæ ventriculi, esophageal and azygos veins, and superior cava. Cases of ascites due to portal obstruction may have severe gastric or esophageal hemorrhages from ruptured varices of these veins.

2. The hemorrhoidal anastomosis is important. The superior hemorrhoidal vein, a tributary of the inferior mesenteric (portal system), communicates with the middle hemorrhoidal, a tributary of the internal iliac (caval system) and inferior hemorrhoidal which empties into the internal pudic. Hemorrhoids are always suspicious of portal obstruction or carcinoma of the rectum.

3. The para-umbilical accessory system of Sappey consists of the inferior and superior epigastric veins, mammary and

diaphragmatic veins, with the umbilical vein in the round ligament of the liver which communicates with the left branch of the portal. This produces the caput medusa about the umbilicus.

4. Colonic and duodenal veins with the left renal.

5. The veins of Retzius connect the intestinal veins by means of retroperitoneal branches to the inferior vena cava.

6. Occasionally the ductus venosus of Arantius remains patent and establishes a portocaval circulation. It is said that cases of portal obstruction or hepatic cirrhosis do not develop ascites when this vein persists.

7. A communication between the portal and phrenic veins sometimes produces fine capillary dilatations along the diaphragmatic attachment to the chest wall. These phlebectasias constitute what has been called Sahli's venous wreath.

8. Exceptional communications exist between the epigastrics, bladder veins, urachal vein (Burow's vein), umbilical, and portal. A left suprarenal communication with the portal has been described by Kutschera.

In caval obstruction the veins of the groin communicate with the lateral abdominal and chest veins (thoracico-abdominal anastomosis). Both portal and caval anastomoses may coexist.

Cardiac and pulmonary hepatic stasis if of long duration usually ends in cirrhosis of the liver with evidences of ascites. If the ascites is extreme, there is an upward displacement of the heart with a torsion of the vessels producing a murmur which disappears with paracentesis. This murmur may be mistaken for that produced by a valvular lesion. The upward displacement of the diaphragm may produce a pulmonary atelectasis, which may be mistaken for a hydrothorax.

III. Inflammation. Tuberculosis of the peritoneum is the most frequent cause of ascites in children. Hepatic cirrhosis in adults is sometimes terminated by a tuberculous peritonitis. Nephritis sometimes terminates with a peritonitis (toxic or infective). In perforative, pneumococcic, or hematogenous peritonitis the pain or rigidity of the abdomen seldom permits of

sufficient manipulation of the patient for the demonstration of free fluid. Ascites may result from an irritative peritonitis from local exudates or inflamed cysts.

IV. Ascites may occur in cachexia, anemia, hydremia, and malnutrition. We have seen a symptomless carcinoma of the stomach in which ascites and generalized edema were the only symptoms. In this case the postmortem failed to reveal any peritoneal or hepatic metastases to account for the ascites, and we concluded that it was of hydremic or marantic origin. Some of our beri-beri cases had ascites which might have been of cardiac origin. Purpura, scurvy, and leukemia are occasionally accompanied by an ascites.

V. Neoplasm. Direct involvement of the peritoneum by a primary or metastatic growth, or implantation metastasis from a papillomatous ovarian cyst, echinococcus, retroperitoneal neoplasm or Hodgkin's disease, and metastatic glands obstructing the portal vein, or hepatic nodules irritating the peritoneal surface of the liver may cause ascites.

VI. Quincke has described an idiopathic type occurring in young girls at the onset of the menstrual function of unknown etiology and of no clinical significance.

The diagnostic deductions to be drawn from a study of the fluid obtained by paracentesis abdominis are as follows:

I. Serous fluid. This may be a transudate from stasis or an exudate of inflammatory origin. After repeated tappings a transudate may become an exudate from a localized peritonitis. Microscopic, bacterial, and chemical studies are necessary for exact diagnosis.

II. Bloody fluid or hemoperitoneum. An injury to a vein from insertion of the trocar must be excluded. The traumatic causes of ascites have been previously considered. Blood may be encountered after a pancreatic hemorrhage, tuberculous or neoplastic peritoneal involvement, from thrombosis of the mesenteric or omental veins, in strangulated hernias and in torsion of cysts or fibroids. It may be present in leukemia, purpura, scurvy, and nephritis with a hemorrhagic tendency. The extravasated blood may form an encapsulated hematocele,

may become calcified, or become pigmented (black) from the hydrogen sulphid present in the bowel.

III. Bile-stained fluid, or choleperitoneum, is evidence of a perforation of the biliary passages or duodenum. From rapid absorption of large quantities of bile by the peritoneum the pulse may be extremely slow and full (Monneret pulse). This coupled with the drowsiness of the patient may be responsible for a failure to recognize a peritonitis.

IV. Chyle and chyliform fluid. The former is the result of an obstruction or rupture of the thoracic duct, receptaculum chyli, mesenteric cyst, or lacteal. The nature of the ingested fats influence the composition of the chyle. If large amounts of butter-fat are consumed, the latter may be recognized in the fluid (Strauss test). A chyliform fluid occurs in degenerating peritoneal neoplasms, or, as described by Musser, after the ingestion of large quantities of milk.

V. In colloid carcinoma of the peritoneum the fluid may be gelatinous, and with a ruptured ovarian cystadenoma the fluid is sticky and mucinous.

VI. Urine may be obtained from accidental puncture of the bladder in paracentesis, or with rupture of this viscus.

VII. Purulent fluid may be obtained when an abscess ruptures into the peritoneal cavity, and with the various types of peritonitis produced by pneumococcus, streptococcus, colon bacilli, etc.

In every case of abdominal distention it is essential to recognize the nature of the distention, and if due to fluid the cause of same and its nature.

CLINIC OF DR. IRVING L. CABOT

METHODIST EPISCOPAL HOSPITAL

USE OF PHENYLHYDRAZIN IN CASE OF POLYCYTHEMIA COMPLICATED BY DIABETES

A WHITE woman, sixty-three years of age, was admitted to the Methodist Episcopal Hospital in 1922. She was then complaining of a cough of fifteen years' duration and of varying severity; dyspnea and weakness of extremities.

The family history was essentially negative except that one brother died of carcinoma of the stomach. The patient had had measles, scarlet fever, tonsillitis, whooping-cough, mumps, and pneumonia in 1917.

At the time of admission she had 4 per cent. sugar in the urine, and a blood-sugar of 330 mgm.; a blood-count of 4,200,000 erythrocytes and 82 per cent. hemoglobin. Diagnosis was made of chronic bronchitis, myocardial degeneration, and diabetes mellitus. At that time her liver was palpable two fingerbreadths below the costal margin. After a month's stay she was discharged on 1306 calories per day, with a urine sugar free and a blood-sugar of 110 mgm.

A second admission in 1924 for similar reasons showed a blood-sugar of 264 mgm. and a blood-count of 6,240,000 erythrocytes with 100 per cent. hemoglobin. Her blood-pressure was 186 systolic and 74 diastolic. On discharge, she was getting 2043 calories per day and had a blood-sugar of 204 mgm. The diagnosis was as on first admission.

At the time of her last admission, in October, 1926, her symptoms were as on both previous admissions. Examination showed a senile type of woman with wheezing respirations and a facies bluish-gray in color. Her tongue was dry and heavily coated and her throat full of mucus.

The heart was enlarged to the left, rapid, the muscular tone poor, no murmurs, and most of the blood-vessels sclerotic. The lungs were full of numerous moist and musical râles. The abdominal wall was relaxed, and there was some distention of the intestines and localized epigastric tenderness. The liver was enlarged to about three fingers below the costal margin, and the spleen not palpable. The musculature of the lower extremities showed marked atrophy and the reflexes were absent or markedly decreased. The eye-grounds showed some clouding and engorgement of all the blood-vessels. The same bluish color was present in the extremities. The blood-pressure was 105 systolic, 80 diastolic. Urine showed a heavy cloud of albumin, acetone, many pus cells and hyaline casts with a few red blood-cells, but no sugar was present. The blood-sugar, however, was 190 mgm. A Wassermann test was negative. A blood-count showed 6,400,000 erythrocytes and 109 per cent. hemoglobin, 6400 leukocytes with 73 per cent. polymorphonuclear leukocytes, and 2 per cent. transitional cells.

Four days after admission she became comatose, and venesection was done, with removal of 360 c.c. blood, with no relief. This had been done on her admission in 1924, with no relief or change in the blood-picture. At this time the blood-sugar was 345 mgm., and 20 units of iletin was given, with apparent good results. She was then established on a dosage of 5 units three times a day, and finally on 15 units three times a day, with a diet of 54 gm. each of protein and carbohydrate and 130 gm. fat until the blood-sugar was reduced to 125 mgm. on November 24th—twenty-eight days after admission.

The diet was then increased to 64 gm. each of protein and carbohydrate and 160 of fat. The blood-sugar fell to 100 mgm. Then the iletin was gradually reduced until, on December 18th, it was stopped entirely, and the patient remained on a diet of 66 gm. each of protein and carbohydrate and 165 gm. fat, or a total of 2013 calories. The blood-sugar was staying at a level of about 107 mgm., and there was no sugar, acetone, or diacetic acid in the urine.

Due to the high erythrocyte count of at least two years'

duration, and the characteristic color of the face, mucous membranes, and extremities we believed this to be a case of polycythemia. Venesection gave no apparent relief in symptoms, appearance, or change in the blood-picture.

Eight days after admission, on November 4th, phenylhydrazin hydrochlorid, gr. ss., was given intramuscularly, followed by gr. iss four times a day intravenously. This was continued until November 12th, making a total of about 48½ grains in an eight-day period, and was according to the technic used in the Mayo Clinic during the past year.

The following blood-counts were recorded:

November 4th.....	Erythrocytes	6,200,000,	hemoglobin	108 per cent.
November 8th.....	"	5,500,000,	"	100 "
November 10th.....	"	5,000,000,	"	90 "
November 12th.....	"	5,000,000,	"	85 "

After the phenylhydrazin was stopped on the 12th of November, the cells continued to drop rapidly the first five days, then remained stationary for twelve days, and then showed a slight increase.

November 17th.....	Erythrocytes	3,400,000,	hemoglobin	68 per cent.
December 1st.....	"	3,415,000,	"	70 "
December 17th.....	"	3,950,000,	"	70 "
December 24th.....	"	4,100,000,	"	76 "

Three days after the phenylhydrazin was first given the patient began to show improvement in appetite, mental acuteness, and general comfort. With the decreasing erythrocyte count her whole condition improved more rapidly, and continued to do so until the only complaints were pain and weakness of the legs.

The color of the mucous membranes and extremities faded, breathing became less dyspneic, and the lungs became clearer. Accompanying this was the marked decrease of blood-sugar which, as stated above, became entirely normal, and the diet was established on an ample caloric intake of 2013 calories, the basal requirement being 1526.

When discharged, on January 1st, the patient was able to walk, although there was marked atrophy of the muscles of the extremities and her only complaint was ascribed to this weakness. At no previous admission had she been so fully relieved of other symptoms, nor had her blood-sugar and diet both been as satisfactory.

Review of the literature pertaining to the use of phenylhydrazin has revealed only two cases of polycythemia with glycosuria, and in these the latter was not a prominent factor. Its use in the case reported above was of undoubted importance in relieving a condition of long standing. The advisability or necessity of such large dosage may be criticised, but it apparently had no alarming effects and, furthermore, has been used in the Mayo Clinic most successfully.

Phenylhydrazin was first used by Hoppe-Seyler in 1885 in an attempt to produce liver lesions experimentally, but, in general, their tests of hepatic function showed no abnormality. Soon after the discovery of acetyl phenylhydrazin (pyrodin) by Liebreich, its derivations were used as therapeutic agents, and chiefly as antipyretics. It was considered that its use was prohibitive, however, because of the toxic effects on the red blood-cells. In 1909 Morowitz and Pratt used phenylhydrazin hydrochlorid to produce secondary anemias in animals, and following this came Eppinger's suggestion that it be used in the treatment of erythremia. Previous to this frequent bleedings had been employed with little effect and *x*-ray or radium treatment had been used on the bone-marrow with equal lack of success.

Minot defines polycythemia vera as a disease due to excessive erythroblastic activity of the bone-marrow, which is comparable to myelogenous leukemia, and he regards them both as neoplasms of hemopoietic tissue. There is apt to be a development of a definite anemia following the early stages of polycythemia, and accompanying this an increase in the size of the spleen. More immature cells appear and a leukocytosis develops as the disease progresses. This is probably dependent on a disorderly proliferation of myeloid tissue, and the fluctuations in

the level of erythrocytes and hemoglobin depend on variation in destruction and formation of cells.

Brown and Griffin, in 1923, studied the nail-fold capillaries which revealed marked engorgement of one or both capillary limbs, the venous side being generally more distended than the arterial. There is a decreased rate of flow in polycythemia and a marked increase in cell and total blood volume.

The use of phenylhydrazin has provoked much discussion as to its effect in the liver in producing a cirrhosis. Levi reports such a case, but it is questionable if the cirrhosis might not have developed had phenylhydrazin not been used. Allen, of the Mayo Foundation, proves quite conclusively in his experiments on dogs that there is little or no evidence of changes in function of the liver or kidneys. The erythropoietic function of the bone-marrow is not changed as was determined by the rate of regeneration before and after its use on dogs. Long, in 1926, noted the increase of reticulated red blood-cells, the phagocytosis of red blood-cells in the blood-stream with the coincident jaundice, and an increase in blood bilirubin after using phenylhydrazin. Urobilinogen and urobilin appeared in the urine as long as there was destruction and there was a slow excretion of the drug in the urine.

Owen, in 1925, discussed the use of phenylhydrazin hydrochlorid and reported some cases of polycythemia in which it was used. These showed the continued destruction of erythrocytes for some time after the drug was stopped, up to a period of two weeks. Inasmuch as a rise in leukocytes always preceded the fall in hemoglobin and red blood-cells, which was accompanied by moderate icterus and urobilinuria, he suggested that this be used as an indication for stopping the drug. The dosage and the length of time required has varied with the individuals using it. Dorsey, of Baltimore, reports cases in which he gave capsules of 0.1 gm. by mouth for twenty days, with intervals over a period of twenty-five months, so that it averaged 0.13 gm. per week. Owen gave 0.2 gm. daily for three or four days, and then 0.1 gm. daily until the leukocytes increased or the hemoglobin dropped below 100. This generally

occurred after two to four weeks, and was followed by giving 0.1 gm. every second or third day.

Long emphasized the advisability of starting with small doses of 0.1 gm. per day by mouth until the red cells begin to drop or until 1 gm. has been given, then to note the cumulative action, and if there is no definite change, give 0.1 gm. alternating with 0.2 gm. daily until the desired effects are obtained.

At the Mayo Clinic larger doses of gr. iss are being used three or four times a day until 3 or 4 gm. have been given. The results obtained are most satisfactory.

Phenylhydrazin exerts a specific effect on the leukocytes and the leukocytosis is not secondary to tissue destruction. Several cases of thrombosis were reported, but this may occur in polycythemia independent of treatment, although it is a question as to whether phenylhydrazin may not be more likely to cause thrombosis in a polycythemic case than in a normal case, as no cases of thrombosis have been reported in normal animals treated with this drug. From all the cases reported, it appears that the drug has no toxic effect and may be used satisfactorily in treating polycythemia.

In the case reported in this article it would be interesting to know the exact relation of this drug to the relief of the pancreatic function, as there was some definite relation of the decrease of erythrocytes and hemoglobin and the ability to utilize carbohydrates. The incidence of polycythemia in this hospital is so rare that study of a considerable number of cases is impossible and general deductions from one case are not justified. In a review of the cases which have been treated with phenylhydrazin and reported we cannot fail to recognize the importance of its use.

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CLINIC OF DR. ARCHIBALD D. SMITH

FROM THE PEDIATRIC SERVICE OF THE BROOKLYN HOSPITAL

INTRACRANIAL HEMORRHAGE OF NEWBORN. REPORT OF SIXTEEN CASES WITH THREE AUTOPSIES

SINCE Sharpe's[1, 2] original report on 500 consecutive lumbar punctures in the newborn, and his conclusion that 9 per cent. of deliveries were complicated by intracranial hemorrhage, much interest has been aroused in the subject, and, like the beginnings of appendicitis, we see more cases because we know what to look for.

The 16 cases here reported have occurred in the obstetric service of Dr. V. L. Zimmerman and associates at the Brooklyn Hospital, and have been transferred to the pediatric service for treatment. All have occurred during the past eighteen months. My thanks are due to my associates, Drs. M. C. Field and H. A. Naumer, and also to Dr. Florence Wilson for their co-operation in reporting them.

Diagnosis.—There are certain conditions clinically in the newborn which have to be considered in making the diagnosis, such as inanition fever and hemorrhagic disease of the newborn.

Inanition fever with its temperature and toxemia may give nervous symptoms, such as twitching, convulsions, etc., simulating intracranial hemorrhage. The diagnosis of inanition fever is helped when we find no symptoms of increased intracranial pressure such as bulging fontanel, and note that the fluid intake has been very limited. In inanition fever the improvement

[1] Sharpe, William: Intracranial Hemorrhage in Newborn, Jour. Amer. Med. Assoc., 81, 620–624, August 25, 1923.

[2] Sharpe, William, and Maclaire, A. S.: Intracranial Hemorrhage in the Newborn, Jour. Amer. Med. Assoc., 86, 332–337, January 30, 1926.

response to fluids subcutaneously or intraperitoneally is prompt and decisive. Frequently, as in Cases 2, 3, 7, 10, 12, and 13, inanition fever and intracranial hemorrhage are associated.

Hemorrhagic Disease of Newborn.—In hemorrhagic disease of the newborn there is usually some trace of bleeding from the skin or mucous membranes or vessels of the cord. These bleedings may occur alone or may be associated with symptoms of intracranial pressure. The bleeding time is increased, and the coagulation time is usually also increased. In Case 1 bleeding time was seven minutes and coagulation time was five minutes. In Case 6 the bleeding time was much beyond twenty-eight minutes and the coagulation time was twenty-eight minutes. In Case 9 the bleeding time was fifteen minutes and the coagulation time was nine minutes.

Poor Nursing.—If a newborn baby has made good attempts at nursing, and then is a poor nurser or refuses the breast, one of the first thoughts is intracranial hemorrhage. This behavior is typical of the beginning of intracranial hemorrhage.

Lumbar Puncture.—When in doubt as to the diagnosis clinically, usually it can be settled by lumbar puncture. A yellow fluid (old blood) or blood-tinged or bloody fluid (not from the trauma of the puncture) settles the diagnosis in cases of doubt.

History.—Something unusual connected with the labor is quite common in intracranial hemorrhage. Three out of the 16 cases were normal spontaneous vertex deliveries. Two out of the 16 cases were breech deliveries, one spontaneous breech, and in the other prolapse of the cord necessitated podalic version with rapid extraction. All of the others varied from easy low forceps extraction to long, hard, dry labor and high forceps. In Case 15 the labor was thirty-nine hours' duration. Case 1 was the second twin to be delivered, the first twin being a stillbirth. In this case also the mother had morphin and ether before delivery, and the baby showed the effects, being blue, and made to breathe only after mouth-to-mouth insufflation.

Symptoms.—The classification of symptoms is made easier if we divide the cases into:

1. Early Cases. (Symptoms coming on at birth or within a few hours of delivery.)

2. Late Cases. (Symptoms coming on from the second to the sixth day after delivery.)

3. Mild Cases.

1. *Early Cases.*—Where symptoms are severe and present from the time of delivery the diagnosis is not often in doubt, but where the symptoms come on gradually the diagnosis is more difficult, and more difficult still is the proper interpretation of the mild cases. Of the early cases, 1, 4, 7, and 9 had *cyanosis* at birth or had attacks of cyanosis. *Twitching* or *tremor* of eyes, lips, or extremities was present from the beginning. *Convulsions* general, or with more pronounced movements in arm and leg of one side were present soon after delivery. *Respirations* in Cases 1, 4, 6, and 7 were irregular in rate and rhythm, and in Case 9 were regular but very shallow and rapid, 96 per minute. *Vomiting* was present in all these cases. *All were too ill to nurse. Lumbar puncture* showed bloody fluid (in all but Case 7) under slightly to moderately increased pressure. In Case 7 lumbar puncture showed amber-colored fluid under slight pressure, and cisterna puncture showed fluid of same character, only thicker.

2. *Late Cases.*—Cases 2, 8, 11, 12, 13, and 14 are illustrative of the later development of symptoms. Case 2 on second day, Case 8 on the sixth day, and the others developing symptoms between the second and the sixth day. Cases 2, 8, 12, and 13 *nursed poorly* or *refused to nurse.* Case 11 was an exception, and nursed well throughout. All had more *vomiting* than usual, except Case 11. Case 8 vomited so persistently that opaque meal and *x*-ray examination were given, which showed, "delay in emptying the stomach (up to four hours), but the meal makes fairly even progress through the pylorus." *Twitching* was present in 4 cases, either eyes, lower lip, hands, or feet. Case 12 had regular *jerking spells,* though no real convulsion. *Cry* was faint and feeble in 3 of the cases. In Case 12 there was a continuous whining. Anterior fontanel varied from depressed to level and full. In Case 13 it was depressed at first and two days later was level, and at the end of a week was bulging.

3. *Mild Cases.*—These cases may present any of the symptoms presented under early or late cases, either singly or in groups. For instance, in one case the only symptom was a bulging fontanel, but lumbar puncture settled the diagnosis as it does in cases under groups 1 and 2. The fluid obtained was bloody.

Pathology.—Autopsies were obtained in Cases 6, 7, and 9. Abbreviated autopsy reports follow:

In Case 6 the report was: "Thymus weighs 15 gm. Cross-section shows minute hemorrhages throughout. Lungs are heavy and dark brown in color. The pleural surfaces are covered with hemorrhages. The stomach shows a few pin-point hemorrhages. The brain surface shows slight congestion and edema."

In Case 7 the report was: "There are a few peritoneal hemorrhages. The thymus weighs 20 gm. The heart shows pericardial hemorrhages. The ductus arteriosus is closed. The serous surfaces of the lungs were studded with small hemorrhages. The spleen weighs 25 gm. The left hemisphere of the brain is covered with blood-clot, particularly on the posterior portion."

In Case 9 the report showed: "Patent ductus arteriosus. There is a wide opening from the pulmonary artery into the aorta. The lungs are air-containing throughout and there are extensive hemorrhages of both pleural surfaces. On opening the brain a great deal of hemorrhage is found under the scalp and over the lateral surfaces of the brain. On opening the ventricles they are somewhat distended and contain dark red watery fluid."

History of Case 6. Lived only a few hours after birth and was hopelessly ill from the start. Spontaneous vertex delivery, weighed 8 pounds, 3 ounces at birth, quite cyanotic from birth, received 20 c.c. of father's blood intramuscularly, anterior fontanel was full, but not tense, bleeding time was more than twenty-eight minutes, clotting time twenty-eight minutes, vomited blood-tinged mucus, respirations shallow and irregular, with lungs aërated, cry fairly strong, but there was continuous

moaning, and extremities and body relaxed. Comparing this clinical history with the autopsy findings, this baby was sicker at birth with congestion and edema of the brain than the other babies with actual hemorrhage.

History of Case 7. Lived two days after delivery. Temperature up to 103° F. Weighed 8 pounds, 10 ounces at birth, was a spontaneous vertex delivery, cyanotic from the first, fontanel depressed, but tense, overriding of cranial bones, not able to nurse at all, had many general convulsions with more movements in left arm and leg, lumbar puncture removed 5 c.c. of amber-colored fluid under slight pressure, and cisterna puncture gave same kind of fluid, only thicker. Comparing the clinical history with the brain-autopsy findings, the interesting fact is brought out that the clot was spread over the left hemisphere and the convulsive movements were more pronounced on the left side (arm and leg).

History of Case 9. A breech extraction, very ill from birth, shrill cephalic cry, respirations regular, heart had gallop rhythm, general convulsions lasting three minutes, frequently repeated, ecchymotic spots on skin, twitching of eyes, made good attempt to nurse at first, then would not nurse and had to be fed by gavage; lumbar puncture gave 10 c.c. bloody fluid under moderate pressure. Bleeding time fifteen minutes, clotting time nine minutes. Anterior fontanel tense and bulging, becoming less tense after lumbar puncture. Received 25 c.c. and again 20 c.c. of father's blood intramuscularly. Weighed 8 pounds, 12 ounces at birth. Lived two days and developed symptoms immediately after delivery. Comparing the clinical history with the autopsy findings, the even distribution of blood over both lateral surfaces of the brain, and the distention of the ventricles with bloody fluid would account for the convulsions with practically no localizing symptoms.

Treatment.—Three problems confront us in the treatment of intracranial hemorrhage of the newborn: 1. To control hemorrhage. 2. To relieve pressure. 3. To supply fluid.

1. To control hemorrhage human blood is the agent of choice and direct transfusion the method of choice. In the Brooklyn

Intracranial Hemorrhage of the Newborn

No.	Name.	Sex.	Labor.	Birth weight.	Twitching.	Convulsions.	Feeding.	Fontanel.	Lumbar puncture.	Bleeding time.	Coagulation time.	Treatment.	Result.	Autopsy.	Diagnosis.
1	Baby R.	M.	Second twin, long, hard, dry labor.	6 lbs., 6 oz.	Right leg, right arm, face.	Many.	Poor feeder. Vomited.	Depressed.	Repeated bloody fluid.	7 minutes.	5 minutes.	Maternal blood clysis.	Recovered.	.....	Intracranial hemorrhage.
2	Baby F.	M.	Medium forceps.	7 lbs., 4 oz.	Left corner of mouth.	.....	Poor feeder. Vomited.	Depressed.	Repeated bloody fluid.	.....	.....	Clysis.	Recovered.	.....	Intracranial hemorrhage.
3	Baby D.	F.	Long dry.	7 lbs., 10 oz.	Tremor lower lip.	Slight.	Nursed well at first, then poorly. Vomited.	Moderately tense.	Very bloody.	1 minute.	4½ minutes.	Maternal blood transfusion 50 c.c. Clysis.	Recovered.	.....	Intracranial hemorrhage. Dehydration.
4	Baby McP.	M.	High forceps.	7 lbs., 6 oz.	Relaxed and blue.	.....	Refused to nurse. Vomited.	Slightly bulging.	Bloody.	.....	.....	Mother's blood 20 c.c. Thromboplastin.	Died.	.....	Intracranial hemorrhage.
5	Baby H.	M.	Rapid extract. High forceps. Prolapsed cord.	8 lbs., 10 oz.	Yes.	Slight.	Vomited.	Tense bulging.	Very bloody.	4 minutes.	7 minutes.	Father's blood 60 c.c.	Died.	Biopsy. Clot right side. Ventricles dist.	Hemorrhagic diathesis. Intracranial hemorrhage.
6	Baby B.	M.	Spontaneous vertex.	8 lbs., 3 oz.	Yes.	.....	Vomited bloody muc.	Not tense.	.....	More than 28 minutes.	28 minutes.	Father's blood 20 c.c.	Died.	Congestion and edema of brain.	Hemorrhagic diathesis. Intracranial hemorrhage.
7	Baby L.	M.	Spontaneous vertex.	8 lbs., 10 oz.	Yes.	Many general.	Not able to nurse.	Depressed, tense.	Amber-colored fluid.	.....	.....	Clysis.	Died.	Clot over left hemisphere.	Intracranial hemorrhage.
8	Baby Y.	F.	Low forceps.	7 lbs., 9 oz.	.....	.....	Poor nurser. Vomited.	Level.	Bloody fluid.	.....	4 minutes.	Transf. 90 c.c. Thromboplastin. Clysis.	Recovered.	.....	Icterus. Intracranial hemorrhage.
9	Baby T.	F.	Breech.	8 lbs., 12 oz.	Eyes.	Many repeated general.	Vomited. Gavage.	Tense bulging.	Bloody fluid.	15 minutes.	9 minutes.	Father's blood 45 c.c. Clysis.	Died.	Blood over lateral surface of brain.	Hemorrhagic diathesis. Intracranial hemorrhage.

10	Baby L.	F.	Medium forceps.	6 lbs., 14 oz.	Arms, legs, eyelids.	.....	Poor feeder. Vomited.	Level and full.	Yellow fluid. Blood tinged.	.....	3 minutes.	Clysis.	Recovered.	.....	Icterus. Dehydration. Intracranial hemorrhage.
11	Baby C.	M.	Spontaneous vertex.	6 lbs., 10 oz.	.....	.....	Nursed well.	Level and full.	Yellow fluid.	.....	.....	.....	Recovered.	.....	Intracranial hemorrhage.
12	Baby W.	M.	Low forceps. Funnel pelvis.	7 lbs., 1 oz.	.....	.....	Poor feeder. Vomited.	Normal.	Yellow fluid.	.....	.....	Clysis.	Recovered.	.....	Dehydration. Intracranial hemorrhage.
13	Baby F.	M.	Medium forceps.	7 lbs., 5 oz.	Tremor lower lip.	.....	Poor feeder. Vomited.	Depressed to bulging,	Bloody fluid.	.....	.....	Clysis.	Recovered.	.....	Icterus. Dehydration. Intracranial hemorrhage.
14	Baby E.	M.	Forceps extraction.	6 lbs., 4 oz.	Yes.	.....	Poor feeder. Vomited.	Level.	.....	4 minutes.	6 minutes.	Clysis.	Recovered.	.....	Intracranial hemorrhage.
15	Baby deM.	M.	Long labor, 39 hours, low forceps.	6 lbs., 12 oz.	.....	.....	Poor feeder. Vomited.	Marked bulging.	Bloody fluid.	Prolonged.	15 minutes.	Transfusion 100 c.c.	Recovered.	.....	Hemorrhagic diathesis. Intracranial hemorrhage.
16	Baby F.	M.	Breech.	6 lbs., 2oz.	Eyes roll, face drawn to one side.	Repeated.	Poor feeder. Vomited.	Bulging.	Clear fluid.	2 minutes.	3 minutes.	.....	Recovered.	.....	Intracranial hemorrhage.

Hospital we are especially fortunate in having a transfusion team, Dr. George G. Cochrane, Jr., and Dr. D. Dexter Davis, whose skill is exceptional and whose methods are machine-like. Transfusion was used in Cases 3 and 8. In Case 3 the direct transfusion of 50 c.c. of maternal blood on the fifth day changed a pale, livid, gasping baby, apparently about to die, into a pink, moving, crying baby, which left the hospital with the mother on the thirteenth day. In this case there was also given on the third day 20 c.c. of maternal blood intramuscularly, and it was repeated on the fourth day, with no stay of the downward progress. In Case 8 a direct transfusion of father's blood on the thirteenth day brought about such improvement that the baby left the hospital on the twenty-eighth day, with no residual symptoms of intracranial hemorrhage and gaining in weight, though not yet back to birth weight. Where transfusion cannot be used we must fall back to the second line of defense, human blood intramuscularly. This was used in Cases 1, 3, 4, 5, 6, and 9. Coagulants can also be used, and in Case 1 coagulen (Ciba) ($\frac{1}{2}$ c.c.) was used, and in Cases 3, 4, and 8 thromboplastin (5 to 10 c.c.) was used.

2. To relieve pressure. Lumbar puncture is the method of choice, and should be used as often as the symptoms of pressure demand it. In the very severe cases it should be done every eight hours until pressure is relieved. Case 8 received 11 lumbar punctures for treatment. When lumbar puncture is unsuccessful, cisterna puncture can be tried to relieve pressure. This was done in Cases 3, 5, and 7. In Case 5 a corpus callosum section was done by Dr. John E. Jennings, and showed a clot on the right side, and cerebrospinal fluid under pressure was obtained from the lateral ventricles. The operation was skilfully and quickly performed, but the baby was very ill and a very poor surgical risk, and survived only a short time.

3. To supply fluid. Babies with intracranial hemorrhage are poor feeders and good vomiters, and as a result, if we are not watchful, inanition fever adds its burden to their illness. To prevent dehydration, and to overcome it when present, normal saline (90 to 100 c.c.) is necessary subcutaneously or intra-

peritoneally. Cases 1, 2, 3, 7, 8, 9, 10, 12, 13, and 14 received normal saline subcutaneously. Case 14 received it five times, and many others three or four times.

The rest of the treatment is symptomatic; proper feeding, breast milk, if available, pumped and fed by gavage if baby is too weak to nurse or use bottle, or a low fat, high carbohydrate milk formula in lieu of breast milk; oxygen inhalations for cyanosis; heart and respiratory stimulation (such as caffein and sodium benzoate, ½ gr. by hypo.), and treatment for convulsions (morphin sulphate 1/60 to 1/20 gr. by hypo., or chloral hydrate ½ to 1 gr. with sodium bromid 2 gr. by rectum or mouth).

Mortality.—Cases 4, 5, 6, 7, and 9 died within two days after delivery. This gives a mortality of 31.2 per cent. for the 16 cases. Before this high mortality rate we are helpless, until we can overcome the hemorrhagic tendency of the newborn and return to the easy labor of the primitive animal.

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MANAGEMENT OF THE ALIMENTARY TRACT IN PNEUMONIA, WITH SPECIAL REFERENCE TO THE DIET AND THE ARTIFICIAL INDUCTION OF BOWEL EVACUATIONS

IN the management of the alimentary tract in pneumonia questions of diet and bowel movements present themselves as fundamentally important. Other questions may also arise in this connection, including those of disturbing medication.

Indications for regulating the diet are suggested by the following facts and considerations.

Pneumonia is a self-limited disease of such short duration that reduction of the quantity of food below the normal health ration, as regards protein content and fuel value, during the active period of the disease, is generally a safe procedure.

From the alimentary tract in pneumonia threaten dangers, particularly to the cardiovascular system, by way of toxemias, disturbances due to visceral distention, and nervous reflex disturbances. These dangers are increased by excessive amounts of food, by food which is difficult or slow of digestion, or which favors the growth in the intestine of the putrefactive types of bacteria; and they are lessened by a diet which is limited in quantity, and consists of fluid articles which are easily digested and of a character that favors the growth of the acidophilic as against that of the saprophytic types of bacteria.

The presence of fever calls for increased rations of alkaline salts to offset the acidic tendency of fever; and the leukocytosis and fibrinous exudation into the lungs call for an increased ration of calcium, to prevent depletion of that important element.

The presence of a specific toxemia, as well as the fever, calls for a large water ration to favor elimination, but, on the other hand, heart weakness may require that the fluid intake be restricted. The unqualified order to "force fluids" can do harm in pneumonia.

The following articles are generally suitable for inclusion in the pneumonia dietary: Modified milk, cereal gruels, strained fresh fruit juices, lactose and dextrose, salts, and particularly those of sodium and calcium, and water. Among the objectionable articles are: Animal broths, raw-egg albumin, and the patent foods which feature the words "peptone" and "peptonoids."

An example of a maximum diet for pneumonia, arranged in accordance with the above suggestions, is given below. It is suitable for cases of average severity which are progressing favorably. It requires modification to meet the varying conditions of the disease and complications.

FULL PNEUMONIA DIET

To be taken through a drinking tube, without raising the head.

At 7 A. M.—A two-to-one mixture of milk with barley water or other specified cereal decoction, 7 ounces (210 gm.), to which has been added sodium chlorid and sodium bicarbonate, of each, 5 gr. ($\frac{1}{3}$ gm.).

At 8 A. M.—Water, 7 ounces (210 gm.), in which has been dissolved calcium chlorid or lactate, 10 gr. ($\frac{2}{3}$ gm.).

At 9 A. M.—The same as at 7 A. M.

At 10 A. M.—The following in a mixture: Strained fresh juice of orange, grapefruit or pineapple, 2 ounces (60 gm.), lactose or dextrose, $\frac{2}{3}$ ounce (20 gm.), and water, 5 ounces (150 gm.).

At 11 A. M.—The same as at 7 A. M.

At 12 M.—The same as at 8 A. M.

At 1 P. M.—The same as at 7 A. M.

At 2 P. M.—The same as at 10 A. M.

At 3 P. M.—The same as at 7 A. M.

At 4 P. M.—The same as at 8 A. M.

At 5 P. M.—The same as at 7 A. M.

At 6 P. M.—The same as at 10 A. M.

At 7 P. M.—The same as at 7 A. M.

Some or all of the fruit-juice feedings may be given in the night time instead of during the day, or the same may be done with the calcium feedings.

This dietetic prescription supplies daily about 38 gm. of protein, about 2 gm. each of sodium chlorid, sodium bicarbonate, and calcium salt, in addition to those salts naturally present in the articles of food given, and about 2700 gm., or 90 ounces, of water, and supplies fuel of a value of about 1200 calories. This diet is considered the maximum; increase in the amount of water is permissible in some cases, but not often is it advisable to exceed a daily fluid ration of 90 ounces, and much more frequently diminution in the amount of fluid is called for.

Modifications of this diet are often required, as in the following conditions:

Modifications of the Full Pneumonia Diet.—When the disease is of severe type, some or all of the milk in the feedings is omitted and barley water substituted. Regularly near the expected time of the crisis the diet is reduced, usually by omitting the milk and restricting the fluid. Often extra fruit-juice feedings are given in place of specified milk and barley-water feedings; and barley water is sometimes given in place of water in the fruit-juice feedings.

If diarrhea or tympanites appear, the diet is reduced temporarily to water, barley water, orangeade, and salts, or to barley water alone.

If signs of heart-failure appear, as rapid pulse, irregular heart action, pulmonary edema, or cyanosis, the fluid intake is diminished and the diet otherwise reduced; usually part or all of the milk is omitted. Omission of all the milk and barley-water feedings in the full pneumonia diet reduces the fluid intake to 42 ounces.

In delirium it is often difficult to get the patient to take food, and effort is directed first to getting water and salts into the patient, then other food.

The sicker the patient, the less food is given. A diet of water and salts, or an alkaline mineral water containing abundant calcium, with strained orange juice and lactose or dextrose, is the diet of safety. Most important are the water and salts.

CATHARSIS IN PNEUMONIA

Hippocrates says: "Artificial evacuations of the bowels, if they consist of such matters as should be evacuated, do good and are well borne, but if not, the contrary." This aphorism implies a condemnation of the use of catharsis as a remedy *per se*. Such use of catharsis, however, in spite of Hippocrates, has been one of the commonest manifestations of meddlesome medicine all down the ages; due, it might seem, to persisting influence of the old doctrine of humoral pathology. The practice of treating disease with catharsis, regardless of whether or not the bowels contain matters that should be evacuated, still has a vogue, and is common in the treatment of pneumonia.

In questioning the advisability of routine catharsis in the treatment of pneumonia, we do not rely altogether on the venerable authority of Hippocrates. The following considerations have suggestive force in this connection.

While a daily evacuation of the bowels in health and with a normal diet is the proper thing, it is observed in conditions of disease that nature not infrequently varies her regular routine as to bowel evacuations. She sometimes permits constipation, and in some cases for an obviously constructive purpose, as in acute appendicitis and peritonitis, and in the later stages of typhoid fever.

With a diet consisting of water, salts, milk, lactose, cereal gruels, and fresh fruit juices, the growth of the acidophilic types of bacteria in the intestine is favored, and that of the saprophytic types more or less discouraged; which means that with such a diet constipation does not carry with it as much of a menace of intestinal toxemia as it would with a diet containing egg albumin and animal broths. Matthews says (Physiological Chemistry, 1925): "None of the products of carbohydrate decomposition are harmful so far as known. . . . By carbohydrate

fermentation acidity is increased. . . . Many bacteria cannot metabolize in the presence of acid. . . . From the decomposition of proteins the most toxic substances are produced."

The administration of a cathartic tends to increase the fluidity of the colonic contents, thereby favoring the multiplication of the bacteria therein and the absorption of toxins through the bowel wall. It has been shown that the bacterial content of the colon is much increased during the first twenty-four hours after free catharsis.

Cathartics, and particularly saline cathartics, by their action may predispose to gaseous distention of the intestine.

Artificial induction of bowel movements tends to produce increased activity of the vagus mechanism, which may have undesirable effects on the cardiovascular system, especially in view of the generally lowered blood-pressure in pneumonia and the often unstable condition of the circulatory apparatus.

The performance of evacuating the bowels by a patient with a weak heart may put him in jeopardy from the physical exertion involved.

It is a clinical observation, as well as an *a priori* deduction, that in pneumonia the dangers from moderate constipation are less than those from routine purgation.

CONSERVATIVE TREATMENT OF CONSTIPATION IN PNEUMONIA

A conservative policy in regard to the artificial induction of bowel evacuations was adopted by the author about fourteen years ago, which may be briefly described as follows:

A necessary condition of this conservative treatment of constipation is that the patient be fed as above described.

If the patient when first seen has not had a satisfactory movement of the bowels within twenty-four hours, and the disease is in a comparatively early stage, and no contraindications are present, particularly cardiac weakness, a soapsuds enema is given, or an enema of a pint of warm water in which has been dissolved a dram and a half of powdered oxgall. After that attempts to move the bowels artificially are not made during the active period of the disease, unless special indications for doing

so appear other than the absence of spontaneous evacuations. Among such special indications are tympanites, which regulation of the diet does not correct, and an uncomfortable sensation in the rectum of which the patient complains. In the author's experience these special indications are of comparatively rare occurrence in patients fed according to the plan above described. It is rather the rule for such patients to show soft abdomens and to be free from abdominal discomfort in the absence of bowel evacuations for considerable periods, especially if the diet is much reduced and the milk omitted from it. It often happens that evacuations of the bowels take place spontaneously, and these natural evacuations do not seem to disturb the patient as much as do the artificially induced ones. Regularly on the second day after defervescence, if the bowels have not moved spontaneously, they are evacuated by an enema. If there should be fecal impaction, as occasionally happens in cases constipated from the beginning or before the beginning of the disease, which was not relieved because of the patient's critical condition, the following procedure is used in the early period of convalescence, and sometimes in protracted cases before convalescence. Six ounces of warm olive oil is injected into the rectum, to be retained, and at the same time 1 ounce of castor oil is given by mouth. Four hours later, if a satisfactory movement has not resulted, the above-described oxgall enema is given. A few hours after the administration of this enema, if the condition calls for it, a colonic irrigation is given. For persistent tympanites, which regulation of diet does not correct, the oxgall enema is given.

CLINICAL OBSERVATIONS

The special dietetic regulation and the conservative management of the bowels above described are essential features of the supportive plan of treating pneumonia, which was gradually developed in the author's experience. Other distinctive features of this plan are: A definite but flexible program of heart stimulation when needed, which employs strophanthin as the principal direct agent; safeguarding of the patient against cold drafts and

chilling, especially when the fever is low and near and after defervescence, and conservative treatment of symptoms. This plan has been described by the author in previous publications.[1]

Statistics of the practical operation of this plan of treating pneumonia are available regarding cases in the author's medical service in the Norwegian Hospital, Brooklyn, New York. Into this service between January 1, 1913 (about which time the conservative policy in regard to bowel evacuations was definitely adopted) and February 1, 1927, excepting the interlude between July 1, 1918 and January 1, 1920, during a large part of which the hospital was used by the United States government for war purposes, came 357 cases diagnosed as lobar pneumonia or influenza pneumonia which were treated according to this plan.

The mortality of this series was 17.6 per cent. Of interest in this connection, and of significance so far as it goes, is the comparison with the mortality of this series, of the mortality of a similar series of 124 cases in the author's service in the same hospital immediately before January 1, 1913, whose treatment differed in some respects, and particularly in that it did not include the conservative policy toward artificial induction of bowel evacuations, from that given to the series after January 1, 1913. The mortality of the earlier series was 30.6 per cent.

Examination of the bedside records of the last 139 cases of the series of 357 cases above referred to, which were in the hospital between January 1, 1920 and February 1, 1927, for the purpose particularly of ascertaining the number of bowel movements which the patients had in the period between admission to the hospital and defervescence, and the number of cathartics and enemas given to them in the same period, and also the incidence of tympanites, reveals the following facts:

Of the 139 cases under consideration, 22 died. Of the remaining 117 cases which recovered, 5 which came into the

[1] New York Med. Jour., January 14, 1911. Long Island Med. Jour., April, 1913. Med. Rec., August 2, 1913. New York Med. Jour., May 30, 1914. Med. Rec., August 28, 1915. Interstate Med. Jour., July, 1916. New York Med. Jour., December 21, 1918. Med. Jour. and Rec., November 15, 1922. Long Island Med. Jour., September, 1926. Med. Times, May, 1927. etc.

hospital at the time of defervescence, or soon after defervescence with delayed resolution, and 10 which showed diarrhea at some time during the active, febrile period of their disease in the hospital, are omitted from consideration. Concerning the remaining 102 cases the following observations are noted. These observations refer to the period between admission to the hospital and defervescence.

No cathartic by mouth was given in any of these cases. In 64 of them neither enemas nor catharics were given. In 38 of them enemas were given. In 28 of them no bowel movements occurred. In 74 of them bowel movements occurred, and in 36 of the 74, in which no enemas were given, bowel movements occurred spontaneously.

The total number of bowel movements in the 102 cases during the active, febrile period in the hospital aggregated 179, and the total number of enemas aggregated 55.

The total number of active, febrile days in the hospital of the 102 cases aggregated 434, giving an average of 4.2 days for each case. The ratio of bowel movements to days was 1 to 2.4—practically one movement to every two and a half days.

Study of individual records shows that 5 of these cases went five days without a movement, that 3 went five days with one movement, that 1 went six days with one movement, that 2 went seven days with one movement, that 2 went seven days with two movements, and that two went eight days with two movements.

The tympanites was noted in 9 cases.

The possibility of errors of observation, and of omission in the records, particularly regarding bowel movements and tympanites, is offset or lessened by the author's general impression of the series: moderate constipation prevailed, and tympanites was not much in evidence, so little so, in fact, as to be scarcely discernible in the composite picture of the series.

COMMENT

We are eagerly expecting an effective biological specific treatment for pneumonia, but that treatment, though bright with

hope, does not seem yet to have emerged from the experimental stage, and there is no effective drug specific treatment of this disease. We are not, however, without therapeutic resources, for we can do much for the patient along the line of physiologic support. Physiologic support does not mean symptomatic treatment, for symptoms do not always call for suppression or modification, being often evidences of reparative activity on the part of the organism; nor does it mean expectant treatment, which may be deficient positively. It means doing things to help the organism in its struggle against the attacking pneumococcus, and refraining from doing things which might impede the natural processes of repair; and it involves resisting influences of tradition and extensive usage which can make for meddlesome medicine.

Opportunities for physiologic support in pneumonia present themselves in the management of the alimentary tract, especially as regards the regulation of the diet and the artificial induction of bowel evacuations. A limited diet of water, milk, cereal gruels, strained fruit juices, milk-sugar, and salts, modified by omissions and reductions to suit particular cases and special conditions, and a conservative policy toward the artificial induction of bowel evacuations, would seem to make for physiologic support and an improved prognosis in this disease.

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GASTRIC SYMPTOMS OCCURRING IN SYPHILITICS

THE presence of a positive Wassermann test in individuals with gastric symptoms may be either purely incidental or evidence of the real cause of the patients' complaints. The gastro-intestinal tract is less affected by syphilis than any other visceral system, the stomach being the least part of the gastro-intestinal tract involved. The rarity of gastric syphilis and the possibility of making a clinical diagnosis with attendant excellent therapeutic results should make one bear in mind at all times the probability of syphilis in individuals who fail to respond to the accepted medical and surgical measure for lesions in the upper abdomen.

No clinical case can be regarded as conclusive even though excellent results follow prolonged and intensive antiluetic treatment. Serologic but particularly *x*-ray study are important aids in establishing a diagnosis which is usually arrived at by a process of exclusion. We must always bear in mind that just as a positive Wassermann reaction may be independent of gastric symptoms and gastric pathology, just so should we remember that a luetic affection of the stomach may exist with a negative Wassermann reaction.

Eusterman, who has enriched the literature by many excellent contributions on this subject, divides the history of the study of gastric syphilis into three periods:

1. Beginning with the study of Chiaris, in 1891, and extending to 1905, during which period postmortem material furnished the basis of all work.

2. From 1905 to 1910, during which time the diagnostic evidence was based on clinical study and therapeutic tests.

3. From 1910 to the present time, when roentgenology and serology largely augment early methods of study.

During the last decade or so many contributions have come from excellent observers, such as Eusterman, Carman, Brams and Bloch, Smithies, Downes, LeWald, Simon, Crohn, Andresen, and others.

Gastric symptoms occurring in syphilitics may be either independent of the luetic infection, or due to either lues of the cardiovascular system, involvement of the nervous system, involvement of the abdominal viscera, or direct affection of the stomach or of other parts of the digestive apparatus.

GASTRIC LUES SIMULATING CARCINOMA (LINITIS PLASTICA TYPE)

Syphilis is generally a tertiary manifestation when it involves the stomach. The characteristic histological changes are usually:

1. Extensive involvement of the blood-vessels with vascular infiltrations and distinct endarteritis and endophlebitis.

2. Marked infiltration of mucosa by plasma and lymphoid cells.

3. The presence of gummata varying in size, or occasionally single, which may or may not ulcerate.

McNee, in 1922, reported the only case in which the finding of spirochetes in the tissue removed from the stomach proved without doubt the syphilitic nature of the lesion. Oppenheim, Crohn, *et al* state, "An organic lesion with a positive Wassermann reaction is only rarely luetic." There is no reason why a luetic cannot develop a carcinoma of the stomach. However, the onset of gastric symptoms in an individual about forty, with clinical evidences of carcinoma, serological evidences of syphilis, and Roentgen evidences of definite anatomic changes in the stomach, should call primarily for active antiluetic treatment before submitting the patient to an operation.

Case Report.—J. C., age thirty-eight, male, married, white, was one of four healthy and normal children, whose previous history was entirely free of any gastric complaints. At the age

of nineteen he had an attack of gonorrhea, but absolutely denies ever having had a primary lesion. The patient has been married fourteen years, and has five normal, healthy children. His wife has had no miscarriages. Gastric symptoms started about two months prior to his first visit (October 12, 1926), with anorexia and epigastric pain immediately after meals. He had lost twenty-three pounds in the last two months. The pain occurred immediately upon taking food, was located in the midepigastrium, did not radiate, and was not relieved by alkalies, but would gradually abate if patient rested. There was no vomiting, an occasional burning sensation, but no nausea. Bowels were regular. There was no distinct aversion to any type of food.

Physical Examination.—Male adult of about forty, of the hyposensitive type, and distinct evidences of recent loss of weight.

The head, neck, chest, abdomen, and extremities revealed no abnormal findings. A soft abdomen made palpation very simple, but no mass could be felt in the epigastrium or any other region. Pupillary reflexes for light and accommodation were normal. All muscle and tendon reflexes were normal.

Laboratory Data.—1. Fasting stomach: about 15 to 20 c.c. of a mucoid material obtained. No free HCl present.

2. Boas-Ewald test-breakfast removed after $\frac{3}{4}$ hour. Free HCl, 0. Total acidity, 0. No blood present at any time.

3. Fractional gastric analysis over a period of two hours failed to show the presence of any acid.

4. Special study after hypodermic injection of histamin failed to show the presence of any free HCl.

5. Gastric ferments were absent on all examinations.

6. Blood study—Wassermann—4 plus. Red blood-count 4,300,000; hemoglobin, 82 per cent.

7. Stool: Benzidin reaction negative on four occasions.

8. Urine: Negative for sugar, albumin, and indican.

9. Wassermann and colloidal-gold reaction were both negative for spinal syphilis. The cytology of the spinal fluid showed no abnormal findings.

Fluoroscopic Examination.—Fluoroscopy of the patient

showed normal lung markings with no change in size, shape, or position of the heart and aorta.

Examination of the stomach while the barium meal was being taken showed a distinct decrease in the tonus, and a marked weakness of the peristalsis. The pyloric region of the stomach showed no peristalsis whatsoever and was distinctly narrow in its lumen, the barium meal leaving the stomach rather rapidly with evident patency of the pylorus at all times.

x-Ray study confirmed the fluoroscopic findings. From the incisura angularis to the pylorus the channel of the stomach was narrowed to almost one-third its usual size. This sausage-like picture was present on all examinations and did not vary either in the upright or prone positions. The stomach was empty in about two hours, with the head of the barium meal in the terminal coils of the ileum and the rest of the meal scattered throughout the loops of the small intestine. Barium-meal was evacuated at the end of forty-eight hours. Barium enema study of colon showed normal findings.

In a discussion of the roentgenology of syphilis of the stomach Carman states as follows: "As a matter of fact, however, the roentgenologist's first suspicion of the lesion being syphilis rather than cancer is usually aroused not by the Roentgen picture so much as by certain obvious clinical facts. There is no absence of palpable mass, the patient may be under the cancer age, he is anemic rather than cachectic, and has not lost weight and strength in proportion to the extent of gastric involvement and the duration of the trouble."

The sudden onset of symptoms in an individual of about forty, in whom there has been no previous history of any gastric symptoms whatsoever, with so marked and rapid loss of weight would, in the great majority of cases, speak for a malignancy. The striking features upon observation, that failed to support the diagnosis of cancer, were the high color of all the mucous membranes and the feeling of general well-being which was not in keeping with the marked loss of weight.

The distinct limitation of the anatomic changes to the pylorus appeared to call for immediate surgery. Since the

definite diagnosis could not be established, the operation was postponed with the consent of the patient, and antiluetic treatment was instituted. Neosalvarsan intravenously, and soluble salt of mercury was given intramuscularly weekly for a period of four weeks. The improvement in the clinical symptoms was manifest after the third week, but the Roentgen examination still showed practically the same findings as on the first examination. Treatment was continued (with decreased dosage) over a period of four months, with gradual improvement in the anatomic structure of the pylorus as evidenced by Roentgen examinations. At the end of six months there was complete restitution of the pyloric region of the stomach to its normal size, shape, and position. The achylia persisted, and has persisted to the present time. The Wassermann has remained strongly positive, and the patient has gained 35 pounds since first coming under observation.

It is important to point out that the clinical improvement followed shortly after antiluetic treatment was instituted. This improvement, of course, may be misleading, for the physician may become unduly optimistic and feel that the local gastric lesion is luetic and not cancerous. The improvement may be a constitutional reaction and in no wise associated with any change in the anatomic defect. In this case, however, treatment was continued with the consent of the patient, who had been given to understand that one could not state definitely whether the lesion was due to cancer or syphilis. Roentgen evidences of anatomic improvement did not follow clinical improvement until a period of several months had elapsed. If the lesion had been carcinomatous a great deal of valuable time would have been lost, and the patient perhaps have reached the stage where surgical treatment would have been of no avail. The patient or the family must at all times understand the exact situation, and know that several months must elapse before one can state with any degree of comfort whether the gastric lesion is or is not luetic.

Merril, in the study of his 16 cases of probable or suggestive cases of syphilis of the stomach, says that there is a progressive course with marked loss of weight, unaccompanied by the degree

of cachexia and weakness seen with cancer. Palpable tumor is uncommon. Schwabel reports a case of carcinoma of the stomach, associated with a positive Wassermann and a history of chancre.

A second patient, fifty-two years of age, male, white, first came under observation about eighteen months ago. He had mild gastric symptoms, but complained chiefly of a diarrhea which had started three weeks prior to his first visit. The pertinent findings after thorough study were:

1. A mass in the region of the rectosigmoid junction.
2. A four plus Wassermann test of the blood.

No tissue was removed from the mass because it was felt that, if it were luetic in origin, improvement would follow specific treatment. If it were carcinomatous the danger of manipulation as pointed out by Buie would be hazardous.

After two months' intensive antiluetic treatment there had been no clinical improvement whatsoever, and, in fact, the symptoms grew worse with an increase of the size of the growth. The patient refused an operation and gradually began to lose a great deal of weight, and subsequently had extensive metastasis to the liver.

In the first case lues is the undoubted cause of anatomic change in a viscus of the gastro-intestinal tract, but in the second case it is simply a coexisting disease. It may at times be exceedingly difficult to arrive at the conclusion as to whether or not syphilis is the cause, or merely the accompaniment of organic structural disease. One may be misled by the clinical improvement which may follow antiluetic treatment. Close observation and study are the only aids at arriving at a proper interpretation. As for syphilis of the stomach, Eusterman states:

"The proof of the specificity of a lesion involves numerous factors. Differential diagnosis is often exceedingly difficult. The requisites are: Demonstrable evidence of a gastric lesion, positive Wassermann reaction or other reliable evidence of syphilis elsewhere in the body, or both, and definite sustained therapeutic improvement. These factors in conjunction with achylia or subacidity in the majority of cases, with the roentgenologic characteristics herein described, in addition to ana-

tomic improvement or cure, seem to make the clinical or intra vitam diagnosis of syphilis of the stomach conclusive."

Marcus reports a case of obstructing lesion of the pylorus in a man of nineteen, who was operated upon and died subsequently. Pathologic examination showed syphilis of the stomach as well as of the liver and kidneys.

Eusterman reports a case of extensive pyloric obstruction in a male adult of thirty-two. Because of the age of the patient and the presence of a strongly positive Wassermann reaction the patient was placed under antiluetic treatment. Within a few months there was anatomic restitution to the normal.

ULCER OF THE STOMACH AND SYPHILIS

Attention has been called by Fowler to the coexistence of ulcer of the stomach and syphilis. This author reports a case in which simple management of a gastric ulcer in a known syphilitic was sufficient therapy to clear up the local condition. Eusterman, on the other hand, reports a syphilitic gastric ulcer which responded definitely to antiluetic treatment. Parody believes that all ulcers of the stomach are luetic in origin. Beebe reports 2 cases of syphilis of the stomach simulating gastric ulcer. Hurst also calls attention to syphilitic involvement of the stomach simulating duodenal ulcer.

It is undoubtedly true that the majority of luetic patients who develop gastric ulcers do not have syphilis as the etiologic factor. The following three patients had definite evidence of a duodenal ulcer, and had a positive Wassermann reaction. Dietetic and therapeutic management and rest in bed brought about a complete cessation of all clinical symptoms.

Case I.—G. F., age 32, male, married, West Indian, gave a history of primary lesion about ten years ago. About five years ago he first began to complain of pain in the epigastrium one or two hours after meals, relieved by the taking of food. During the past five years he has had recurrence of symptoms every four to five months, relieved by alkaline medication. Patient was first seen in October, 1924, and since then has had only

two attacks of gastric pain after dietetic indiscretions. Attention to proper diet and alkalies gave immediate relief. The Wassermann has been positive at all times, and patient has been receiving antiluetic treatment at regular intervals.

Case II.—B. C. V., age thirty-eight, male, married, American, gives a history of recurrent gastric pain over a period of two years, occurring usually in the fall and winter months. Pain was in the midepigastrium two to three hours after meals, associated with marked heart-burn. History of primary sore thirteen years ago. Wassermann reaction strongly positive.

Case III.—J. P., age forty, male, married, American, gives a history of gastric symptoms for fifteen years, pains coming on usually one to two hours after meals, recurring about once a month. During last six months has been having night attacks which were relieved by taking small amounts of milk. History of luetic infection six years ago, with treatment during last two years. Wassermann remains weakly positive (2 plus).

All three patients presented normal figures in their gastric chemistry. Only in one was there a high rise in acid value at the end of two hours.

x-Ray showed definite evidence of duodenal ulcer in all three patients. There were no abnormal findings in the nervous symptoms of any of the patients which might lead one to suspect luetic involvement.

All antiluetic treatment was stopped during the period of active clinical symptoms, and prompt relief was brought about by the usual treatment instutited for duodenal ulcer.

Even though good results are obtained without the aid of antiluetic treatment, one cannot state definitely that a luetic ulcer of the duodenum may not also respond favorably to the usual treatment, though all specific therapy be omitted.

Mortimer, in 1917, reported a case of syphilis of the duodenum based on the marked improvement of the duodenal lesion which followed only after antiluetic therapy.

From a roentgenologic standpoint the anatomic changes in

the duodenum may be alike in the syphilitic and simple ulcer. Should improvement occur after specific treatment, it would be hazardous to assume a diagnosis of syphilis of the duodenum, because the constitutional reaction may be responsible for the clinical improvement.

Despite the specific treatment that these patients have been receiving during the last few years, the Roentgen evidences of duodenal ulcer are practically unchanged during all examinations. It is also interesting to note that *x*-ray examination during the quiescent stage reveals but little changes of the duodenal bulb from what is seen during active symptoms.

HEMATEMESIS IN LUETICS

The vomiting of blood is always of grave concern both to the patient and to the physician. The striking thing about these two patients whose cases are cited below was the apparent well-being at the time of the attacks of vomiting, and the absence of any gastric symptoms at any time prior to or between the attacks.

The positive Wassermann reaction gave us the only clue as to the possible cause of vomiting blood. It might be interesting to know how many patients with so-called essential hematemesis may not really be luetics. Even in the so-called essential vomiting of blood there may be an interval of freedom between attacks that may last for months. Not infrequently an innocent appendix and a normal gall-bladder may be blamed as the cause of the gastric hemorrhage, just because the blood Wassermann is negative.

Case I.—Female, thirty-six years of age, came under observation about five years ago for vomiting of blood. She had had three attacks of hematemesis six months prior to the first visit.

Physical examination showed no abnormal findings. Blood Wassermann was positive. Roentgen examination of the stomach failed to reveal any changes in the form, size, shape, or position of the organ. No history of any gastric crisis. The patient's well-being, the absence of any gastric symptoms whatsoever, and

the presence of a 4 plus Wassermann made us feel that lues was probably at the basis of the entire picture. Antiluetic treatment was instituted. Since then her family doctor tells me that she has had no attack. It has been a matter of five years now since the patient first came under our care, and there has been no history of any gastric symptoms or gastric distress or bleeding at any time since then.

Case II.—A. C. M. Male adult, forty-one years of age, had been in perfect health until he came under observation two years ago because of sudden onset of vomiting of blood. There had been a history of a chancre twelve years previously. Physical examination failed to reveal any abnormal findings in the throat, lungs, abdomen, or in the nervous system. Blood Wassermann was positive. Two weeks following the first attack of hematemesis patient again vomited about 8 ounces of blood. He was put to bed for a few days, and antiluetic treatment was instituted. He was under observation for a period of six months and had no recurrence of the bleeding. Roentgen examination of the gastro-intestinal tract was negative.

TABES DORSALIS AND GASTRIC SYMPTOMS

There are many bizarre gastric symptoms that arise when lues involves the nervous system. The occurrence of gastric symptoms in an individual with recognizable tabes dorsalis gives the physician a sense of security in ascribing the epigastric pain, discomfort after meals, vomiting, etc., to the changes in the nervous system. Not infrequently, as pointed out by Fremont-Smith and Ayer, two types of mistake in the diagnosis are possible:

1. "Tabes dorsalis may not be recognized, and the symptoms attributed to an intra-abdominal pathologic condition, or—

2. Tabes dorsalis only may be recognized and an accompanying ulcer disregarded."

These authors made a study of 50 cases of neurosyphilis in which gastro-intestinal symptoms were prominent. In this group 12 patients were operated on under mistaken diagnoses.

It may be exceedingly difficult at times to differentiate the coexistence of an ulcer in the presence of definite tabes. It seems, however, more difficult to establish a diagnosis of tabes when there are but a few suggestive signs in the nervous system and where the symptoms of ulcer persist and recur, and where the clinic and *x*-ray fail to show conclusive proof.

Case I.—H. A. P., male, adult, forty-seven years of age, Italian, married, first came under observation about seven months ago. His chief complaint was burning pain in the epigastrium coming on one to two hours after meals, with a slight relief upon the taking of alkalis. There was a history of gastric symptoms over a period of two years, with free intervals of from one to three weeks with variability of the time of the onset of pain, which ranged from fifteen minutes to two hours after meals. This was not dependent upon the type of food, but nevertheless resembled that associated with duodenal ulcer, so as to make the diagnosis of ulcer of the duodenum strongly suggestive. *x*-Ray examination of the stomach and duodenum showed a hypertonicity and hyperperistalsis, but no direct evidence of ulcer of the doudenum. Fluroscopic and *x*-ray examination were repeated on three occasions during the course of one month, but the diagnosis of duodenal ulcer could not be verified. Study of the gastric chemistry by fractional method showed a normal acidity curve. The blood Wassermann examination was negative and the patient denied the history of a chancre. Neurologic examination showed no abnormal findings. In view of the persistence of symptoms and the failure to respond to the usual treatment, and in the absence of positive Roentgen findings a spinal tap was done and the Wassermann returned 2 plus. The patient was put under antiluetic treatment and there was a gradual improvement of his clinical symptoms.

This case represents that type of mild tabes with gastric symptoms that go from clinic to clinic and not infrequently are operated upon with unfavorable results. In this patient we find a train of gastric symptoms extending over a period of two years. In spite of the accepted therapeutic procedures the patient

failed to respond, and a diagnosis was not established until a spinal Wassermann was done. Spinal puncture is not the routine office procedure, but undoubtedly the more frequent use of this examination would help to clear up the diagnosis in many an obscure case.

Case II.—A. S., age fifty, male adult, American, single, came under observation about five months ago. There was a gastric history over a period of two years. Chief complaint was pain in the upper abdomen, especially on the left side, which came on two hours after meals and was not relieved by the taking of alkali. Rest in bed and local applications of heat would give little relief. Heartburn was a troublesome symptom, and occasionally there was regurgitation of sour material. Bowels were costive. There was no history of any attacks which simulated that of gastric crisis. Roentgenologic examination showed marked increase in the peristaltic activity and tone of the stomach. There was no evidence of ulcer either of the stomach or duodenum on repeated examination. Fractional analysis over a period of two hours showed a persistent hyperacidity and hypersecretion. Blood Wassermann was negative on two occasions. The presence of Argyll-Robertson pupils and the absence of knee-jerks pointed to a syphilitic involvement of the nervous system as the probable cause of the gastric symptoms. A spinal tap was done on two occasions and the Wassermann returned negative. Neurologic evidence of syphilitic involvement of the nervous system became more marked, so that we felt that beyond a shadow of a doubt tabes dorsalis was responsible for all of the gastric symptoms.

Case III.—W. J. M., age forty-one, male adult, American, married, has been under observation for the last eighteen months. He has given a history of a duodenal ulcer symptom-complex for the past four years. *x*-Ray examination shows definite evidence of an ulcer of the duodenum. There is a history of syphilis contracted fifteen years ago. Blood Wassermann is weakly positive and the spinal fluid shows a 2 plus Wassermann reaction.

There are no Argyll-Robertson pupils present, but the knee-jerks are absent, and in the last few months the patient has had attacks of pain in the upper abdomen which bear no relation to meals and appear to be associated with the changes in the nervous system.

In the first patient we have a history suspicious of duodenal ulcer, normal roentgen findings, normal blood serology, and a 2 plus Wassermann of the spinal fluid. In the second patient we find a bizarre gastric symptom-complex, normal Roentgen findings of the gastro-intestinal tract, normal serology both of the blood and spinal fluid, but definite clinical involvement of the nervous system. In the third patient we find evidence of both lues of the spinal cord and the presence of a duodenal ulcer.

The diagnosis of tabes dorsalis may at times be exceedingly difficult, particularly if the neurologic findings are meager, and the serology fails to give any clue to the underlying cause. It is this type of patient that is often operated upon without success and who subsequently presents the real nature of the complaints. On the other hand, as Fremont-Smith and Ayer point out, tabes dorsalis may be recognized and an ulcer disregarded. They cite a case in which perforation of a duodenal ulcer took place in an individual who had tabes dorsalis.

To make a diagnosis of ulcer of the stomach or duodenum as due to lues is highly presumptive, for, as Kwartin and Heyd have recently shown in a detailed histologic study of 3 cases with peculiar ulceration of the stomach suggesting lues, "it is not possible to determine the exact nature of such lesions from their anatomic and histologic appearance without the demonstration of etiologic organisms."

SUMMARY

1. Direct involvement of the stomach by lues is a rare occurrence. The fact that it does occur demands careful study of every patient with gastric anatomic changes, particularly if the age of the individual is under forty. Clinical improvement in gastric syphilis on antiluetic treatment usually occurs in a much shorter time than does anatomic restitution.

2. A simple peptic ulcer may occur in luetics and respond to ordinary management. Improvement on antiluetic treatment may be due to a constitutional reaction, and does not prove the lesion to be specific.

3. Vomiting of blood may be the only symptom or sign of syphilis. In the presence of a positive Wassermann reaction the diagnosis may be relatively simple. Surgical intervention in the so-called essential hematemesis should not be resorted to until lues can be definitely excluded.

4. Tabes dorsalis in its early stages may produce so bizarre a gastric symptomatology as to make a positive diagnosis difficult. With advanced tabes, or in the presence of a positive serology, the diagnosis is usually simple. A peptic ulcer, however, may be present in a tabetic patient. More frequent application of spinal puncture may help to establish a diagnosis of tabes when upper abdominal symptoms persist and resist all forms of treatment.

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LIPOID-CELL SPLENOHEPATOMEGALY, NIEMANN-PICK TYPE. A CLINICAL ANALYSIS OF 9 CASES WITH A REPORT OF ONE ADDITIONAL CASE

Historical Review.—In 1882, Gaucher[1] described a new type of splenic enlargement caused by the accumulation of masses of large pale cells. Additional cases were subsequently described by Picou and Ramond,[2] Risel,[3] Schlagenhaufer,[4] Cornil,[5] Collier,[6] and others. Bovaird,[7] followed one case for thirteen years when postmortem examination revealed the nature of the condition. Schlagenhaufer's patient lived for thirty-nine years after the disease was recognized. Until 1921 no case had been reported in an infant. The youngest patient was a boy, reported by Mandelbaum in 1913.[8] In a recent monograph, Pick[9] was able to collect 39 authentic cases.

The pathology of this disease has been studied by Gaucher,[10] Bovaird,[7] Mandelbaum and Downey,[11] Epstein,[12] Pick,[9] and others. Brill[13] was first to make the diagnosis during life. In collaboration with Mandelbaum and Libman he called attention to certain distinctive clinical phenomena, namely, the chronicity of the malady, its racial and familial preference, the cutaneous pigmentation with its peculiar distribution and the changes in the conjunctival mucous membranes. Although Mandelbaum and his collaborators[8] observed isolated groups of Gaucher cells in the bones of their patients, gross lesions of the bones have been described only recently by Howland and Rich,[14] Pick,[9] and by Welt, Rosenthal, and Oppenheimer.[15]

Until 1914 all cases of splenohepatomegaly, showing large pale cells in the spleen and liver, bone-marrow, and lymph-nodes,

were considered to be Gaucher's disease, although students of the pathology of this disease recognized that some of the material differed microscopically from the classical picture.

In 1914, Niemann,[16] under the title "Ein unbekanntes Krankheitsbild," described a peculiar form of splenohepatomegaly occurring in an infant, which was fatal at eighteen months of age. Niemann had no first-hand knowledge of the histology of Gaucher's disease. He states, "Originalpräparate eines Gaucherschen Falles habe ich zwar nicht gesehen, nach der Beschreibung und den der Publikationen beigegebenen Abbildungen scheint es sich aber um ganz dieselben Zellen zu handeln, die bei der Splenomegalie Gaucher nicht nur in der Milz, sondern auch in Leber und Drüsen gefunden werden." From a study of the text and illustrations from the literature, he felt that the cells found in his case resembled those described by Gaucher, but he believed his case to be, at least clinically, different from Gaucher's disease because of its early onset and rapid progress.

In 1916, Knox, Wahl, and Schmeisser[17] reported 2 cases of splenohepatomegaly, occurring in sisters of Jewish parentage. Both terminated fatally before the end of the second year. The organs showed masses of cells which resembled but were not identical with those of Gaucher's disease. One of these patients showed retinal changes pathognomonic of Tay-Sachs disease.

In 1921, Siegmund[18] reported a case of "lipoid-cell hyperplasia of the spleen," in a nine-months-old infant. He considered the condition an early stage of Gaucher's disease. The histologic similarity between the two forms of splenohepatomegaly stimulated attempts to establish chemical differences. Siegmund carried out some chemical studies of the liver and spleen and compared the results with those obtained on normal organs. The amount of material extractable with ether, alcohol, and chloroform was greater in the diseased organs. Lieb[19] succeeded in isolating from Gaucher material a cerebroside which he identified as kerasin. This substance Epstein and Lieb[20] considered peculiar to the Gaucher cells. Recently, Bloom and Kerr[21] made a careful study of the chemical composition of a normal

spleen, of one obtained from a case of Gaucher's disease, and of one from a patient with Niemann-Pick disease, and added 3 cases of the latter condition to the literature. The total amount of ether extract of cholesterol and its esters, and of organic phosphorus derived from phosphatids, was much higher in the spleen of the patient with Niemann-Pick disease than in the Gaucher or the normal spleen. Schiff[22] has reported an increase of lipoids and cholesterol in the blood. Hamburger's[8] patient also showed hypercholesterolemia.

The retinal changes of amaurotic family idiocy have been observed in 3 cases, one described by Knox, Wahl, and Schmeisser, one by Bloom, and a case observed by Hamburger and briefly described by Pick. We desire to record a fourth case, belonging to this group of so-called Niemann-Pick splenohepatomegaly with amaurotic family idiocy, and to present a clinical summary of previous cases.

Clinical History.—*Patient*: E. L., female, white, age fourteen months, Hebrew, admitted February 27, 1927, died March 20, 1927.

Chief Complaint.—Large spleen since four months of age. Failure to gain weight, and retarded mental development.

Family History.—Father, twenty-seven, salesman, living and well; mother, twenty-two, housewife, living and well; are first cousins. Patient is only child and only pregnancy. Family history otherwise negative.

Previous History.—Full term, forceps delivery; no convulsions, cyanosis, desquamations, eruptions, icterus, petechiæ, or fever.

Feeding.—Exclusively breast-fed for nine months. On admission was receiving whole milk, cod-liver oil, orange juice, cereals, eggs, vegetables, mashed liver, and prune juice.

Development.—Held head up at three months. Has never stood up. Does not speak. Dentition: first and only tooth appeared at one year.

Present Illness.—Four months ago baby had a cold, was taken to a family physician who discovered a large spleen. Child failed to gain weight consistently. Was unable to sit

up without support at ten months. *x*-Ray treatments were advised and given, but the child became so weak that they had to be discontinued.

Physical Examination.—A poorly nourished infant with a rather large head and an enormous abdomen.

Measurements.	Patient, inches.	Normal average, inches.
Length	28	28
Head circumference	18½	17¾
Chest circumference	17½	17¼
Abdomen circumference	21¼	16¾

Cervical lymph-nodes just palpable. Other lymph-nodes not palpable. Heart and lungs negative. Throat negative. Tonsils small. Over the lumbar and sacral regions there are large, dark blue areas—so-called mongol spots.

Abdomen.—Large, protuberant, with marked fulness in the flanks, especially on the left side. There is a mass on the left side, extending from beneath the costal margin almost to Poupart's ligament. The anterior border of this mass extends almost to the midline, and has a notch about two finger-breadths above the umbilicus. The liver edge is almost 3 inches below the costal border, in the midclavicular line. Examination of the eye-grounds reveals cherry-red spots in both eyes at the site of the macula lutea on a white background. These findings were confirmed by the ophthalmologist, Dr. I. A. Feldman.

The hopelessness of the condition was explained to the parents, but it was admitted that a fatal termination could possibly be deferred for a few months by splenectomy. The parents insisted that this be carried out in the hope that some unexpected beneficial result might follow.

March 5, 1927: Splenectomy by Dr. John Linder.

March 16, 1927: Child developed pneumonia of the right upper lobe.

March 17, 1927: Bleeding from the right nostril. A culture showed diphtheria bacilli. Five thousand units of antitoxin were given intramuscularly, and the child was transferred to the Kingston Avenue Hospital, where it died forty-eight hours later.

Laboratory Data.—Bleeding time, six minutes; coagulation time, three and a half minutes. Clot retraction time, forty-five minutes. Fragility-hemolysis of red blood-cells began at 0.46, and was complete at 0.28. Blood Wassermann negative. Tuberculin 5 mg. negative. Cholesterol, 137.5 mg. per 100 c.c. blood. Fasting blood-sugar, 114.5 mg. per 100 c.c. blood. Bilirubin: direct, negative; indirect, 1 unit. Icteric index, 4.5. Urine negative.

	February 27, 1927.	March 13, 1927.	March 14, 1927.
Hemoglobin	68%	62%	
Erythrocytes	2,810,000	2,720,000	
Color index	1.2	1.1	
Leukocytes	5,800	5,400	12,600
Polymorphonuclear neutrophils	46 %	53 %	68 %
Eosinophils			
Basophils			2 %
Lymphocytes	54 %	47 %	30 %
Platelets	192,000	220,000	

12/14/26: Red cells somewhat paler than normal, with some microcytosis.

1/14/27: Red cells show anisocytosis (4 to 10 microns) and occasional polychromatophilia.

Roentgenograms of the skull and long bones showed diffuse osteoporosis, but no focal bone-resorption.

Pathologic Report by Dr. Max Lederer.—The spleen weighs 480 gm.; is pinkish in color, and retains the contour of the normal spleen. Microscopically the splenic tissue is almost completely replaced by masses of large, pale cells, of varying shape but well-defined borders. The nuclei are small when compared with the size of the cell, usually single and eccentrically placed. The protoplasm is very granular. Vacuolization is almost entirely absent. The cells stain well with lipoid reagents, but fail to respond to neutral-fat stains. These cells have almost completely replaced the splenic follicles. Here and there remnants of these follicles, consisting of islands of lymphoid cells, are still visible. The sinuses are dilated in some sections and completely collapsed in others. The dilated sinuses show a few red blood-cells, but are entirely devoid of the characteristic large, pale cells. A

more complete description of the spleen will appear in a subsequent communication.

Chemical Analysis.—Chemical analysis of the spleen yielded the following results:

	Mean per cent.
Moisture (loss on evaporation)	74.3
Ether extract (dry spleen)	30.5
Alcoholic extract	27.0
Ether-insoluble, extracted matter*	8.4
Acetone precipitate	2.7

* Material in the residue obtained on evaporation of the ether extract which failed to redissolve in ether.

The concentration of ether-soluble material approximates very closely that reported by Bloom and Kerr as characteristic

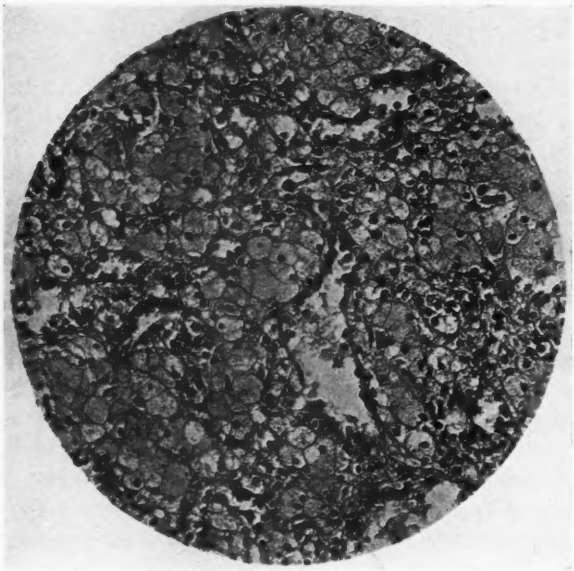

Fig. 134.—Showing characteristic cells, same magnification, with dilated splenic sinus containing occasional red blood-cells, but no foam cells.

of Niemann-Pick disease, and is much higher than that found by the same authors in a case of Gaucher's disease. We have not

ventured into a complete quantitative chemical study of our material, but for the present have been content with the demonstration of its richness in ether-soluble substances.

Whether we are dealing with a form of Gaucher's disease beginning very early in infancy, or a separate disease entity, is still a mooted point. The older observers were inclined to consider all cases of splenohepatomegaly, due to the presence of

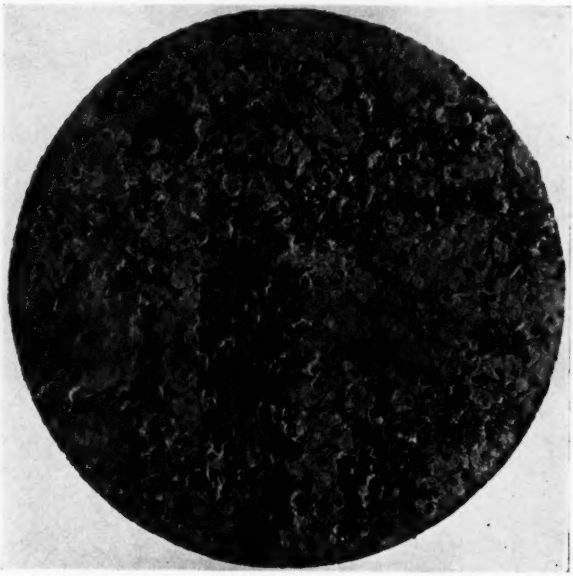

Fig. 135.—Showing masses of large, pale cells with eccentrically placed nuclei, and remaining groups of lymphoid cells between cell aggregates.

large, pale cells in the spleen and liver, as Gaucher's disease. Niemann thought that the histology of his case so closely resembled that of true Gaucher, that one could only conclude that the same pathological process may exist with a variety of conditions which are clinically different. Siegmund considered his case of lipoid splenohepatomegaly an early stage of Gaucher's disease. Knox, Wahl, and Schmeisser felt that the concept of Gaucher's

disease should be made broad enough to include their cases, but Mandelbaum and Downey were unwilling to recognize at least one of the cases reported by Knox, Wahl, and Schmeisser as Gaucher's disease. They stressed the histological differences between the two types of cells, and the very wide-spread distribution of the cells in lipoid splenohepatomegaly as compared with their restricted localization in the spleen, liver, bone-marrow, and lymph-nodes in Gaucher's disease. Attention should be called to the frequent association of Tay-Sach's disease with lipoid-cell splenohepatomegaly, an association hitherto never observed with an undoubted case of Gaucher's disease.

Clinical Analysis of Cases.—An analysis of the cases in the literature reveals the criteria upon which the clinical diagnosis rests. We have succeeded in collecting 9 authenticated cases, and have added one case. The previously reported cases have been discussed exhaustedly by Pick in his recent monograph. Of the 9 cases, 3 were reported by Bloom, 2 by Knox, Wahl, and Schmeisser, one each by Niemann, Schiff, Hamburger, and Siegmund. There were seven girls and two boys. In one instance the sex is not given. The ages varied from five to seventeen months. They were all white. Seven of these were Jewish children. In the remaining 3 cases no statement is made as to the patient's race. The disease may be present at birth or may appear as late as the tenth month. None of the patients survived the second year. Moderate enlargement of the cervical and axillary lymph-nodes was observed in a few instances, but general lymph-node enlargement is usually absent. The enlargement of the abdomen was the outstanding feature. This was due for the most part to splenic enlargement, and to a lesser degree to enlargement of the liver. A moderate degree of anemia was present in every instance. The majority of patients showed a moderate leukocytosis which in time was replaced by a leukopenia. A reduction of the platelets appeared late in the disease in some of the cases. Two patients showed an increase of the cholesterol concentration of the blood. Retardation of mental development was present in a majority of the patients. Our patient could not sit alone at ten months. In 3 instances mental

Name.	Age.	Sex.	Color.	Race.	Reported by	Age at onset.	Age at death.	Family history.
E. L.	14 months.	F.	White.	Hebrew.	Kramer-Lederer.	4 months.	15 months	Parents first cousins. other pregnancy.
C. K.	16 months.	F.	White.	Hebrew.	Wm. Bloom, Amer. Jour. Path., vol. I, November, 1925, p. 595.	Present at birth.	16 months.	.....
.....	15 months.	F.	White.	.....	Hamburger, rep. Pick, L. Erg. D. In. Med. u. Kind., vol. 29, p. 519, 1926.	.....	.....	Sister died at 1 ye Splenic and hepatic e largement.
.....	17 months.	M.	White.	Hebrew.	E. Schiff, Jahr. f. Kind., 1926.	3 months.	.....	Negative.
S. G.	5 months.	F.	White.	Hebrew.	Knox, Wahl, Schmeisser, Bull. Johns Hopkins Hosp., vol. 26, p. 60, 1915.	5 months.	16 months.	Sister—S. G.
S. G.	9 months.	F.	White.	Hebrew.	Knox, Wahl, Schmeisser, Ibid.	.....	11 months.	Father, 41, Mother, well; 11 children, 6 we Patient youngest. I fant sister, 5 month same condition.
B.	14 months.	F.	White.	Hebrew.	Wm. Bloom, Amer. Jour. Path., vol. I, 1925, p. 595.	8 months.	21 months.	.....
W. K.	7 months.	M.	White.	Hebrew.	Wm. Bloom, Amer. Jour. Path., vol. I, 1925, p. 595.	7 months.	7 months.	.....
I. D.	.....	..	White.	.....	Albert Niemann, Jahrb. Kinderheilk., vol. 79, P. L., Jan., 1914.	2 months.	17 months.	.....
Unknown	9 months.	F.	White.	.....	Siegmund, Verhandl. d. Deutsch. Ger. Path., vol. 18, 1921, p. 59.	.....	.....	Sister died at 1 year large liver and spleen.

NOTE: The limits in the number of leukocytes for all observations as well as the limits of variation of the percentage of

SUMMARY I

TEN CASES LIPOID-CELL SPLENOHEPATOMEGALY (Niema

ry.	Symptoms.	Physical examination.	Eye examination.	Laboratory tes
ns. No .	Failure to gain properly and develop normally. Large spleen discovered at 4 months. Gradually fading eyesight. Nystagmus.	Poorly-nourished, large head, enormous abdomen. Length, 28 inches. Head circumference, 18½ inches. Chest, 17½ inches. Abdomen, 21¼ inches (Normal, 16¾ inches). Large, blue spots over the lower back. Cervical lymph-nodes palpable. Huge liver and spleen.	Transverse band of pupillary remnant runs across right pupil. Cherry-red spots in both macular regions surrounded by large, circular, white areas. Disks, pale.	Blood Wassermann tive. Tuberculin negative. Chol 138 mg. per cent. ing blood-sugar, per cent. Bilirub rect, negative; rect, 1 unit. Ict dex, 4.5.
.....	Stationary weight. Diarrhea and under-development. Pneumonia. Blood and mucus in stools.	Poorly nourished, anemic. Red macular rash on face and thorax. Cervical lymph-nodes, palpable. Lungs, few râles. Abdomen, distended and tense. Enlarged liver and spleen.	Not done.	Von Pirquet and mann, negative.
1 year. atic en-	Enlarged abdomen. Anemia.	.....	Cherry-red spots on macula lutea.	Wassermann, nega
	Enlarged abdomen.	Enlarged abdomen, loss of weight, pale brown pigmentations of hands and face, mild rickets. Enlarged submaxillary glands below angle of lower jaw. Geographical tongue. Large liver and spleen.	No record.	Tuberculin and mann, negative.
	Always thin and sickly. Weakness and emaciation.	Large abdomen. Emaciation. Dilated superficial abdominal veins. Large, firm spleen and liver. Palpable cervical lymph-nodes. Enlarged inguinal and axillary lymph-nodes. Slight lateral nystagmus.	Bright red area in region of each macula. Disk, white with indistinct margin.	Von Pirquet test, tive. Radium ments followed duction of le count from 11, 2360.
her, 38, , 6 well. st. In- months,	Never thrived. Vomiting.	Emaciation and pallor. Slight brown pigmentation of skin. Prominent abdomen. Cervical and axillary lymph-nodes enlarged. Soft systolic murmur at apex. Large liver and spleen.	No record.	Wassermann and Pirquet tests, neg
.....	Retarded development.	Anemic and deformed. Pupils do not react to light. Conjunctivæ, subicteric tint. Upper eyelids swollen. Fine nystagmus of both eyes. Breathing obstructed, tonsils enlarged, lips pale. Cervical lymph-nodes, palpable both sides lower thoracic. Spine kyphotic, ribs flared out. Abdomen prominent. Bilateral talipes. Left hand locked distal phalanges of four fingers. Epiphyses of all bones enlarged.	.....	.....
.....	Cough. Fever.	Well nourished. Acutely ill. Rapid respiration. Marked nystagmus. Spleen enlarged, liver palpable. Convulsions, face and right arm. Turbid spinal fluid, showing Pneumococcus Type II. Kernig and Babinski signs positive. Both upper extremities spastic.	.....	.....
.....	Abdominal enlargement. Improper development. Difficult feeding.	Under-nourished, retarded development, mental and physical. Wide open fontanel Failure of all static functions. Pale brown pigmentation of face, bluish areas below twelfth dorsal. Obliquity of the eyes suggesting mongoloid type. Navel obstruction. Abdominal circumference, 50 cm. Abdominal veins dilated. Edema of feet and eyelids.	.....	.....
year of pleen.	.....	Large liver and spleen, moderate anemia. Urine—albumin, sugar—negative.	.....	.....

age of each type of white blood-cell are given. * mg. per cent = mg. in 100 c.c. of whole blood.

SUMMARY I

TEN CASES LIPOID-CELL SPLENOHEPATOMEGALY (Niemann-Pick)

	Eye examination.	Laboratory tests.	Blood.*	Cause of deat
s abdomen. rence, 18½ omen, 21¼ blue spots mph-nodes	Transverse band of pupillary remnant runs across right pupil. Cherry-red spots in both macular regions surrounded by large, circular, white areas. Disks, pale.	Blood Wassermann, negative. Tuberculin, 5 mg., negative. Cholesterol, 138 mg. per cent. Fasting blood-sugar, 114 mg. per cent. Bilirubin: Direct, negative; indirect, 1 unit. Icteric index, 4.5.	Red blood-cells, 2,720,000 to 2,819,000. Hemoglobin, 68 to 72 per cent. White blood-cells, 5800 to 12,600. Polymorphonuclears, 46 to 68 per cent. Lymphocytes, 30 to 54 per cent. Bleeding time, 6 minutes. Coagulation, 5½ minutes. Clot retraction, 45 minutes. Fragility, normal. Platelets, 192,000 to 220,000.	Nasal and pha diphtheria. B pneumonia.
ar rash on s, palpable. ended and	Not done.	Von Pirquet and Wassermann, negative.	Red blood-cells, 4,860,000 to 4,900,000. White blood-cells, 19,650 to 36,000. Hemoglobin, 70 to 90 per cent. White blood-cells, 9100. Neutrophils, 28 to 53 per cent. Small mononuclears, 54 to 34 per cent. Large mononuclears, 8 to 10 per cent. Transitionals, 3 to 4 per cent. Eosinophils, 1 to 2 per cent. Basophils, 2 per cent.	Pneumonia.
.....	Cherry-red spots on macula lutea.	Wassermann, negative.	.....	.....
ale brown ld rickets. angle of arge liver	No record.	Tuberculin and Wassermann, negative.	Red blood-cells, 4,600,000. White blood-cells, 10,800. Lymphocytes, 49 per cent. Platelets, 20,000. Marked lipemic turbidity of serum. Cholesterol, 620 mg. per cent. Hemoglobin, 70 per cent. No polychromasia anisocytosis and poikilocytosis. Bleeding and coagulating time, normal. Fragility, normal. Blood-serum, 6.7 per cent. protein.	.....
ed superspleen and des. Enmph-nodes.	Bright red area in region of each macula. Disk white with indistinct margin.	Von Pirquet test, negative. Radium treatments followed by reduction of leukocyte count from 11,240 to 2360.	Red blood-cells, 3,240,000 to 4,608,000. White blood-cells, 6480 to 23,600. Hemoglobin, 65 per cent. Polymorphonuclears, 34 to 77 per cent. Lymphocytes, 60 per cent. Transitionals, 1 to 3½ per cent. Eosinophils, 1½ per cent. Myelocytes, 3 per cent.	Exhaustion.
pigmenta- Cervical Soft sysnd spleen.	No record.	Wassermann and von Pirquet tests, negative.	Leukocytes, 10,400 to 25,400. Red blood-cells, 4,400,000 to 5,200,000. Hemoglobin, 90 to 60 per cent. Polymorphonuclears, 42 per cent. Large mononuclears, 3.2 to 5 per cent. Small mononuclears, 36 to 41 per cent. Myelocytes, 1 per cent.	Exhaustion.
t react to . Upper both eyes. rged, lips able both ribs flared al talipes. s of four ed.	.....	.....	Fragility of red blood-cells, normal. Red blood-cells, 3,560,000 to 4,200,000. White blood-cells, 23,400. Hemoglobin, 45 per cent. Neutrophils, 40 to 45 per cent. Small mononuclears, 37 to 42 per cent. Large mononuclears, 8 per cent. Transitionals, 7 per cent. Myelocytes, 3 per cent. Moderate anisocytosis, poikilocytosis, polychromatophilia. Bleeding time, 6½ minutes. Blood cholesterol, 210 mg. per cent. Blood fatty acids, 640 mg. per cent. in serum.	.....
espiration. liver palrm. Turcus Type ve. Both	.....	.....	Hemoglobin, 65 per cent. Red blood-cells, 3,960,000. White blood-cells, 29,200.	Purulent me Pneumococcus T
t, mental Failure pigmentath dorsal. bloid type. mference, Edema of	.....	.....	.....	Diarrhea.
. Urine—	.....	.....	.....	Pneumonia.

00 c.c. of whole blood.

f death.	Weights, liver and spleen.	Organs involved.	Diagnosis by.	Treatment.
pharyngeal Broncho-	Spleen, 480 gm.	Liver and spleen. Others not examined.	Splenectomy.	Splenectomy.
	Liver, 580 grams. Spleen, 190 grams.	Liver, spleen, thymus, lungs, mesenteric lymph-nodes, glomeruli of the kidney. Cortex of the adrenals. Mucosa of the small intestines.	Autopsy.	None.
.....	Spleen, 310 grams.	Liver, spleen, lymph-glands, bone-marrow, glomeruli of kidney.	Splenectomy.	Splenectomy.
.....	.....	.....	Splenic puncture.	None.
	Liver, 410 grams. Spleen, 100 grams.	Thymus, lungs, spleen, liver, adventitis of adrenal vessels, adrenals, kidneys, mucous membrane of gastro-intestinal tract. Lymph-nodes, bone-marrow, brain.	Biopsy. Lymphatic glands from neck and axilla. Autopsy.	Radium.
	Liver, 425 grams. Spleen, 86 grams.	Liver, spleen, inguinal glands. Lungs, large pale cells in alveoli. Adrenals, thymus.	Autopsy.	None.
.....	Spleen, 268 grams.	Liver and spleen. Others not examined.	Splenic puncture. Splenectomy.	Splenectomy.
meningitis. cus Type II.	Spleen, 62 grams. Liver, normal in size.	Thymus, alveoli of lung, spleen, liver. Mucosa and submucosa of duodenum. Mesenteric lymph-nodes. Adrenals. In the branches of the renal artery. Bone-marrow, only an occasional cell.	Autopsy.	None.
	Very large, not weighed.	Liver, spleen, lymph-glands, kidneys, adrenals.	Autopsy.	None.
	Spleen, 310 grams. Liver, weight not given.	Lymph-nodes, liver, spleen, bone-marrow, kidneys, vascular endothelium, skin, heart.	Autopsy.	

SUMMARY II

DIFFERENTIAL DIAGNOSIS OF GAUCHER AND NIEMANN-PICK SPLENOHEPATOMEGALY

	Gaucher's.	Niemann-Pick.
Number of cases..	39	10
Age at onset.....	8 months to 56 years—1 at 12 months, 1 at 8 months.	Symptoms usually first noticed during first six months.
Sex.....	39 cases, 14 males.	10 cases, 2 males.
Duration.....	2 to 39 years.	Always fatal before end of second year.
Organs involved..	Confined to liver, spleen, bone-marrow, and lymph-glands.	Brain, spinal cord, liver, spleen, bone-marrow, lymph-glands, blood-vessels, kidneys, adrenals, intestines.
Eyes.....	Pinguecula on scleræ and conjunctivæ.	Cherry-red spots in macula lutea of both eyes, 4 cases in 10.
Histology.....	Negative to lipoid stains. Cells contain hemosiderin and iron. Linear striations of cytoplasm.	Cell reaction strongly positive to lipoid stains. No hemosiderin or iron. Vacuolated cytoplasm.
Chemistry.....	Ether extract: cholesterol and cholesterol esters, small amount. Alcohol extract: small amount. Organic phosphorus: small amount. Contains kerasin.	Cholesterol: large amount. Ether extract: large amount. Alcohol extract: large amount. Organic phosphorus: high.
Blood-count.....	Leukopenia. Normal or reduced platelets.	Slight leukocytosis followed by leukopenia. Normal or reduced platelets.
Blood chemistry..	Normal.	May have lipemia and hypercholesterolemia.
Skin.....	Diffuse and patchy pigmentation partly about neck, face, upper extremities. Wedge-shaped thickening of conjunctivæ (pinguecula).	Mongoloid spots, diffuse brown pigmentation, particularly about face.
Development....	May be normal for years.	Retarded in both physical and mental development.

retardation was due to an associated amaurotic family idiocy. Our patient could still follow light when first seen, but subsequently developed nystagmus and complete blindness. In 4

cases another member of the family had died of splenic enlargement during the first year of life.

Pathologic Physiology.—Little is known regarding the nature of this disease. That it is not a disease of the spleen alone is evident from its pathology. Even early cases show the lesion to be wide-spread. Pathologists have focused their attention upon the origin and staining reactions of the cells in the hope of establishing differences between these cells and those of Gaucher's disease. There has been much controversy as to whether they are derived from the endothelium lining the splenic sinuses, from the lymphoid cells of the follicles, or from some other tissue. All such controversies are no longer pertinent since the work of Aschoff and his pupils.[24] It is now generally accepted, thanks to these investigators, that the remarkable cells of this disease and those of Gaucher's disease are derived from the reticulo-endothelial system. There is some evidence that the cells of the reticulo-endothelial system participate in the elaboration of antibodies and in the metabolism of lipoid substances and cholesterol.

The cells of the reticulo-endothelial system have a number of functions. These include, among other things, the storage of vital dyes, colloidal-iron particles, blood and biliary pigments and their derivates, and lipoids including cholesterol and its ester. Reticulo-endothelial cells, superficially resembling those of Niemann-Pick disease, proliferate when diets rich in lipoids and cholesterol are fed to animals. Similar cells may be found as large aggregates in organs, particularly the spleen and liver, in fatal cases of diabetic lipemia. The presence of lipemia and hypercholesterolemia in a number of cases of Niemann-Pick disease suggests that here also we are dealing with some disturbance of lipoid metabolism, and the finding of large amounts of phosphatids, cholesterol, and cholesterol esters in the cells themselves constitutes additional evidence in favor of this hypothesis. The frequent association of Niemann-Pick disease with amaurotic family idiocy, a disease having its beginnings early in intra-uterine life remains to be explained.

Differential Diagnosis.—It is doubtful whether a diagnosis

of lipoid-cell splenohepatomegaly can be made during life, in the absence of the morphologic changes in the eyes or the chemical changes in the blood. The diagnosis has been made by splenic puncture followed by examination of the material for the characteristic "foam cells." The brown pigmentation of the skin may be mistaken for jaundice, and a diagnosis of hemolytic familial jaundice made. True jaundice is usually absent. The splenic enlargement in hemolytic familial jaundice seldom reaches the degree which obtains in Niemann-Pick disease. The red blood-cells show normal resistance to hypotonic salt solutions in the latter condition. Although Niemann's case gave a positive Wassermann reaction, he did not consider the condition syphilitic, and this represents the consensus of opinion today. The Wassermann reaction in all subsequent cases has been negative and the histologic picture does not suggest syphilis. The condition may be confused with aleukemic leukemia, secondary anemia, or von Jaksch's pseudoleukemia. The presence of an increased concentration of lipoids and cholesterol in the blood is suggestive of some metabolic disturbance analogous to that produced by Anitschkow[23] in animals by feeding diets rich in lipoids. It recalls the lipoid cell infiltration of the spleen, liver, and other organs, seen in fatal cases of diabetic lipemia. These facts have suggested the hypothesis that the process is a disturbance of lipoid metabolism, in which lipoids, cholesterol, and cholesterol esters are stored in the cells of the reticulo-endothelial system, the latter having undergone a marked proliferation. The association of a rapidly growing spleen, in a female infant of Jewish parentage, associated with Mongol spots and amaurotic family idiocy makes up a clinical syndrome which cannot be missed if one is familiar with the condition. In the absence of these diagnostic criteria, splenic puncture or biopsy must be resorted to. We have classed our case as belonging to the type described by Niemann-Pick. Clinically it certainly belongs to this group. However, it differs histologically from the classical picture. The cells show no vacuoles, and the lipoids are not soluble in the ordinary lipoid solvents. Chemical analysis shows the material to be much richer in ether soluble substance than the spleen of

Gaucher's disease. Epstein has stated that the cells of the two diseases may be indistinguishable microscopically. In Gaucher's disease the sinuses often contain the characteristic cells, which can also be seen growing from the endothelium lining these spaces. This finding was lacking in our case. We could not obtain an autopsy and were, therefore, prevented from studying the distribution of the cells in organs other than the spleen. The clinical diagnosis of our patient is, therefore: Lipoid-cell splenohepatomegaly (Niemann-Pick type), Tay-Sachs' disease, secondary pneumonia, nasal and pharyngeal diphtheria.

Prognosis and Treatment.—There is a striking difference between the prognosis of this disease and that of the classical Gaucher's disease. The latter, as stated before, is a chronic disease. It is not incompatible with a fair degree of health for years. Not infrequently the discomfort of the large spleen is the only thing causing the patient to seek relief. Many years elapse between the removal of a Gaucher spleen and the final fatal termination. In contradiction to this picture we have the rapid progress of Niemann-Pick disease. No case has survived the second year of life. Bloom thought that splenectomy prolonged the life of the patient, but the child succumbed before the article describing the case was off the press. Radium and x-rays have both been tried with unsatisfactory results.

Conclusions.—A summary of the clinical findings in 9 cases of Niemann-Pick disease taken from the literature and one added case has been presented. The clinical syndrome of splenohepatomegaly, beginning in infancy with Mongol spots and amaurotic family idiocy, has been confirmed. The differential diagnosis between this condition and the classical picture of Gaucher's disease has been discussed.

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CLINIC OF DR. TASKER HOWARD

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COMPENSATION AND REPAIR. SOME CLINICAL EVIDENCE BEARING ON OPTIMISM IN PROGNOSIS

IN a posthumous paper of the late Dr. L. Emmett Holt,[1] that wise physician pointed out the remarkable possibilities for repair in growing children, and related case histories, drawn from his long experience, describing serious damage in early life with complete functional restoration. He emphasized the universal tendency toward healing while the organism is in the stage of evolution, and made rational an optimism which faces frank pathology and dares to hope for complete recovery. Dr. Holt suggested that others who might have the opportunity of following the course of events over many years in regard to various types of patients should more often make public the result of their observations. It is with this in view that the following case histories are reported, and, as in Dr. Holt's paper, they are frankly selected because of the favorable outcome in the face of a discouraging outlook at the start. Some of them are still diseased, and seriously so, but they must be classified as reasonably comfortable and efficient.

Case I. Nephritis, with Albuminuria Persisting Six Years.—V. Z., an Italian iron moulder, in 1911, at the age of eighteen, suffered an acute nephritis with anasarca and heavy albuminuria. I saw him almost yearly for fifteen years, and for six years watched a persistent albuminuria. During this time his blood-pressure ranged from 120 to 140. For the following nine years his urine was free from albumin. He never was the type in whom one might expect to find the orthostatic albuminuria of youth, and

it seems fair to assume that the albuminuria was due to the nephritic damage, which ultimately cleared up. It may recur, but it is doubtful whether he is more prone to nephritis than if he had never had it. At all events, it seems that an albuminuria due to nephritis may persist for six years and then remain absent for at least nine years.

Case II. Adenitis, Splenomegaly, Diverticulitis.—In 1911 W. B. was three and a half years old. His teeth were very carious, and one after another became infected and had to be extracted. The lymph-glands in his neck became as large as chestnuts. They tended to vary somewhat in size. The removal of apparently infected tonsils had no effect upon them. He was subject for several years after this to attacks of fever, and an erythematous eruption which resembled German measles. These attacks would last several days at a time. His second teeth came in on schedule and were normal in appearance. In 1916 he began to complain of abdominal pain, rather indefinite in its distribution, the cervical glands became larger, and the spleen was palpable. He had some nausea and an irregular fever of 99° to 101° F., which persisted for six weeks. At this time frank consolidation appeared at the right apex, and it seemed as though tuberculosis were probably the explanation of the whole picture. A sleeping porch was built at the rear of their city house and the boy has slept out of doors ever since. The lung involvement soon disappeared, but the adenitis with a tendency to fever toward night and to night-sweats persisted for four months. He then began to have attacks of diarrhea in addition to his other troubles. Soon after this there were added periods of angioneurotic edema, about the face, neck, and chest. During this period there was a tendency to a slight leukocytosis. His urine, Wassermann, and von Pirquet were negative. His stool showed a preponderance of streptococci. More abscessed teeth were found and infected tonsillar tags removed. The spleen was sometimes felt and sometimes not. The association of the angioneurotic edema, with spells of diarrhea, suggests that the abdominal symptoms might have been due to a protein sensi-

tization. It is quite possible that this factor was responsible for some of the attacks of abdomoinal pain and diarrhea, particularly as on one occasion an eosinophilia of 8 per cent. was demonstrated. However, many of the attacks were more protracted than those usually seen with food sensitization, and were accompanied by fever, which is unusual in that condition. Furthermore, the course of events pointed in another direction. For six years he suffered frequent recurrences of the symptoms—periods of fever and diarrhea with a persistence of the adenopathy. His schooling was seriously interfered with, and he was reduced to semi-invalidism. He was admitted to the Long Island College Hospital in 1922 for study. The stool still yielded many streptococci. An *x*-ray of the digestive tract, made by Dr. A. L. L. Bell at this time, showed the presence of 3 diverticuli in the colon. He was given periodical doses of castor oil followed by barium sulphate, with an occasional irrigation, Bacillus acidophilus cultures, and milk-sugar. The diarrhea promptly subsided, but he was kept in bed for several weeks on a very bland diet. The temperature soon subsided and he gradually regained his strength. He has had no recurrences and he has developed into a vigorous muscular youth.

It would seem that the story of this boy presents an illustration of a prolonged struggle against the streptococcus.

Case III. Rheumatic Endocarditis.—Mrs. L. F., a strong, vigorous woman of thirty-five, sent for me in July, 1923, suffering from an acute tonsillitis. Her sister has a mitral stenosis of rheumatic origin. The patient has never had rheumatism, although she had had scarlet fever and pneumonia as a child. On examining her I was surprised to find the typical signs of a mitral stenosis—a clean-cut presystolic roll and snapping first sound. She went back to her country place before she should have, and was told by a physician there that she had serious heart disease. I saw no more of her for a year, when she reported for some minor complaint. She explained that she had had her tonsils out in the fall as directed and had been remarkably well ever since. Examination failed to show the slightest sign of

any trouble with her heart. Four years later her heart still appears quite sound. It is not suggested that the tonsillectomy cured her mitral stenosis. She must have had a rheumatic vegetation on the valve when first seen, and this appears to have healed without leaving a trace of its former existence. Four years is time enough to show some sign if that valve is destined to deformity.

Case IV. Diabetes Mellitus, Pernicious Anemia, Cholelithiasis.—In 1921 Mr. B., a man of sixty-three, began to be troubled with polyuria. His urine was found to contain 4.7 per cent. of glucose, and the blood 833 mg. per 100 c.c. This was just at the time of the publication of Newburgh and Marsh's[2] first paper on the high fat, low protein, and low carbohydrate diet. The patient was put on a diet of 10 gm. protein, 96 gm. fat, and 14 gm. carbohydrate, and told to report with a twenty-four-hour specimen for an estimation of the sugar output. Much to my surprise, when he returned in five days, the urine was normal in every respect. He has had only an occasional trace of glycosuria since. For six months the blood-sugar ranged between about 150 and 250 mg., indicating a high threshold. Many times since then it has been as low as 100 mg. The protein allowance was higher than the Newburgh figures after the first week, averaging 100 to 120, while the fat seldom exceeded 150. The carbohydrate was kept at about 70. In other words, our patient proved to have a mild type of the disease in spite of the high sugar values first encountered. He never has shown any acidosis.

However, in 1924, it became evident that something ailed him beside his diabetes. He began to look pale, and to complain of dyspnea on exertion and swelling of the ankles. A blood-count showed changes suggesting pernicious anemia, hemoglobin 53 per cent., red blood-cells 1,800,000, white blood-cells 7000, index 1.48, many macrocytes and poikilocytes, polychromasia, and one normoblast. Later studies showed a fairly constant leukopenia and many times megoloblasts, beside the usual high-color index.

He received the usual treatment of the times, including sunshine, arsenic, hydrochloric acid, and the removal of some badly infected teeth, but showed very little change for about six months, when he suddenly became very much worse. His hemoglobin dropped to 20 per cent., his red cells to 568,000. He was febrile, edematous, and semicomatose, and was admitted to the Long Island College Hospital. His condition seemed desperate. However, a month in the hospital, with four transfusions (direct method) set him on his feet again, and he was discharged with a hemoglobin of 60 per cent.

During the next eighteen months the patient required transfusions twenty-six times, making thirty transfusions in all. He had several partial remissions, which he would hold for a few months and suddenly relapse. One notable feature was the constant tendency to fever that he exhibited. Out of 22 admissions to the hospital there were only 4 in which fever was not recorded, not including the slight posttransfusion temperature which is usually seen. The fever was most marked with the higher grades of anemia and tended to disappear with improvement. Such fever in pernicious anemia is an occasional finding. The patient's spleen was inconstantly palpable, tending to disappear with improvement. The fever, with splenic enlargement and the positive indirect van den Bergh, which we have so frequently found at Long Island in pernicious anemia, seem to me to indicate a hemolytic process during the relapses of this disease. The recent suggestion of Minot and Murphy[3] that the anemia is due to inhibition of maturation in the bone-marrow does not seem sufficient to explain the picture.

During this eighteen-month period the patient had three attacks of common-duct obstruction, lasting only a few days, but each presenting a very stormy aspect. With a high fever he always became delirious or semicomatose and extremely prostrated, and this was the state of affairs with each attack. The gall-bladder was readily felt, and a slight jaundice developed. The association of gall-bladder disease and pernicious anemia has long been noted. The patient was one of three exhibiting this combination whom I observed that year. In the

case of one of the others, a woman, the illness began with a frank cholecystitis. Since gall-bladder infection has been urged as a cause of pernicious anemia, a surgeon was asked to remove this woman's gall-bladder, which he did. The bile and the gall-bladder were both sterile. Histologically, there was not a suggestion of inflammation. Many of the cells were infiltrated with lipoid substance. It was a typical strawberry gall-bladder. The operation had no effect on the course of the anemia. It seems much more probable that the correlation of these diseases is due to a disturbance of the cholesterol metabolism. In pernicious anemia, and in diabetes as well, the blood-cholesterol typically runs high. The last reading on Mr. B. was 225 mg. per 100 c.c.

A new period began for our patient at the end of eighteen months, when he was placed upon the high liver diet of Minot and Murphy.[4] His hemoglobin was fast slipping and had reached 41 per cent. He was given another transfusion, his last, and this raised it to 50 per cent. After two weeks of the liver diet it was 62 per cent., in four weeks 70 per cent., in eight weeks 90 per cent. His clinical improvement was as striking. He has remained sugar-free, though his last blood-sugar reading was 200 mg., on a diet of approximately 150 to 200 gm. of protein, 70 to 100 gm. of fat, and 70 to 100 gm. of carbohydrate. The last blood-count, taken eight and a half months after the inauguration of this régime, was hemoglobin 98 per cent., red blood-cells 4,496,000, white blood-cells 7300. He feels quite well and thoroughly enjoys himself, having retired from business.

Case V. Angina Pectoris, Aortic Regurgitation.—In June, 1924, Mr. W. S., a mechanical engineer of sixty-five, reported complaining of pain in the chest, coming on after exertion and radiating down the arms. His pains in the chest had begun in 1912, and as they usually occurred within a short time after meals he consulted a gastro-enterologist, who, after a thorough gastro-intestinal review, treated him for nervous indigestion. The pains gradually became worse, and about 1915 he noticed that when the pain was unusually severe it would radiate down both arms. The attacks were most apt to occur if he walked

soon after eating. They were accompanied by considerable apprehension, and at times with some breathlessness. By 1924 he could not walk two blocks without bringing on an attack. An electrocardiogram, taken six months previously, had shown evidence of definite cardiac pathology, and he had learned that the attacks were promptly controlled by nitroglycerin.

A physical examination showed a normal blood-pressure. The heart was normal in size, but there was a systolic murmur at the base and an accentuated aortic second sound. The radials were somewhat beaded. The liver was slightly enlarged and the epigastrium a little tender. The Wassermann and urine were negative.

An electrocardiogram showed slurring of the R wave in Lead II, and notching in Lead III. The T wave was inverted in Leads I and II.

In the years that he has been under observation, the left border of his heart has shifted from 10 cm. to 12.5 cm. from the midline. Corresponding with this there has developed in the electrocardiogram the evidence of a left preponderance. It is interesting to note that the main deflection downward in Lead III seems to be an exaggeration of the notching noted in the R of Lead III several years before. The wave seems to be invaginated and ultimately turned wrong side out. In the course of the development of a left preponderance, R3 should theoretically grow gradually smaller, disappear, and then reappear inverted and increase to a maximum. The notched appearance of R3 in the series of tracings shown is probably an accidental addition to this evolution, representing a slight deflection of the direction of the excitation wave, caused by some local ventricular pathology. However, it is recorded for comparison with similar studies in the development of preponderance. Quite recently, since the detection of the hypertrophy and the left preponderance, it was found that by direct auscultation a faint diastolic murmur was audible down the left of the sternum. This could not be heard with a stethoscope. The blood-pressure readings also show a large pulse-pressure, averaging 140 mm. over 60 mm. There is evidently developing some leakage of the aortic valve.

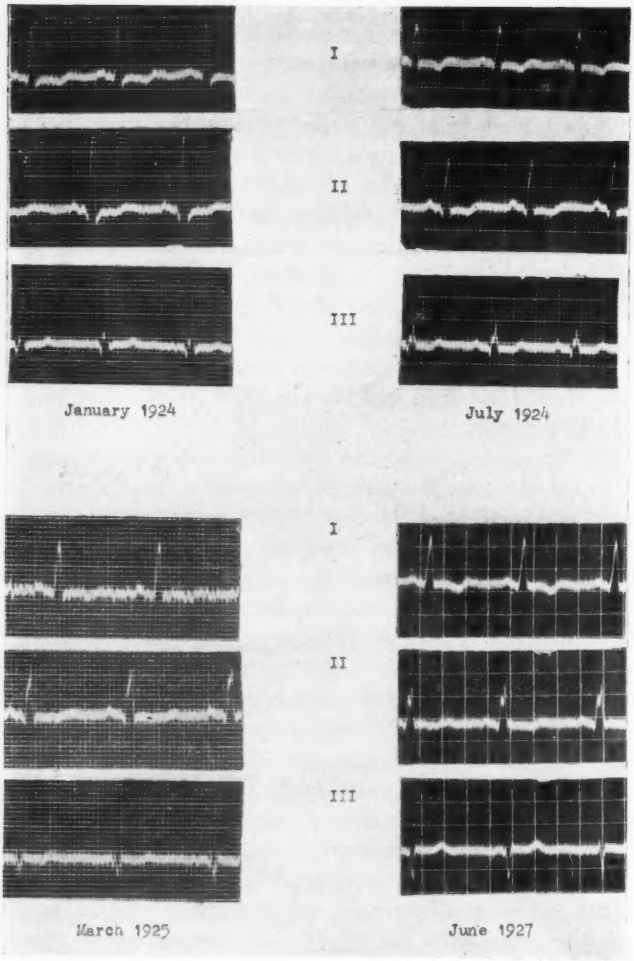

Fig. 136.—Case V. Note slurring and notching in R2, inversion or diphasic deflection in T1 and 2, and the evolution of a tracing representing left preponderance, with the apparent invagination of the main deflection in the third lead.

So far as the pain goes, in the three and a half years that have passed there has been little change in the tendency to the attacks. Drugs seem to have but little effect, even nitroglycerin losing considerable of its power to help him. If he keeps still he can remain quite comfortable, but for a greater part of the time he has done everything but keep still. He has repeatedly taken long business trips alone in his car, driving one to two hundred miles a day. He has been abroad five times spending months directing litigation for his firm in Germany and in England. He has deliberately chosen to pursue a life of considerable activity in spite of the resulting discomfort and risk. It is now fifteen years since he began to have attacks of angina pectoris, and he is still carrying on.

Case VI. Arterial Hypertension, Angina Pectoris, Complete Heart-Block.—At the age of forty-three, Mr. M. reported because a life insurance examiner had told him that his blood-pressure was a little too high. This was in 1917. He had previously been rated up because of some condition of the heart. He was a short, stocky man of ruddy complexion. His blood-pressure read only 158 mm. systolic and 88 mm. diastolic. His heart, however, showed a definite enlargement to the left, a rough systolic murmur being audible at the base and into the neck, at the apex, and around into the axilla. The valve closure sounds were ringing. The urine was free from albumin and showed a concentration of 1030.

He was not seen for four years when he came in complaining of precordial pain. For six months he had been subject to rather mild attacks of pain starting in the left side of his chest, running through to the back, into the left shoulder and down the left arm. They were always brought on by exertion and were most apt to occur after breakfast on his way to business or if he walked after dinner. There was no particular change in his physical examination except that the blood-pressure had dropped to 149 mm. over 98 mm. He was advised to take a vacation and generally lower the tension of his life. Three months later he reported that he was having but very little pain.

He was not seen until 1924, when he came in explaining that he planned to be married and thought he would be examined to see if he was all right. Examination showed a blood-pressure of 195 mm. over 90 mm., a heart that was still further enlarged, and a pulse rate of 40. This was found to be due to a complete heart-block. He was advised not to marry. Have you ever advised against an immediate marriage?

He reported after the honeymoon and again three and a half years later. He is still placidly going about his business, playing an occasional game of golf, and climbing four flights of stairs to get to his apartment. If he hurries he has some cardiac

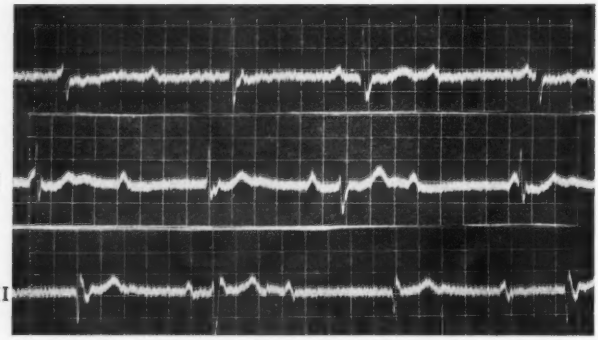

Fig. 137.—Case VI. Complete heart-block. left preponderance, extra systole in Lead II.

distress. His systolic blood-pressure is over 200 mm., and his heart-block is still present. Otherwise he is all right.

It is not unusual to outlive the start of hypertension by over ten years, or angina pectoris by six, or heart-block by three and a half. The combination is perhaps deserving of record. The man who calmly disregarded all three, embarking on the adventure of matrimony and sailing serenely on, certainly is so deserving.

Cases have been cited illustrating repair or reserve powers in the heart, kidneys, arterial system, bone-marrow, colon, and pancreas. Remarkable instances of lung repair are too common to excite comment. May I, however, relate an instance that

occurred in the practice of a friend of mine in Philadelphia, the son of a long line of physicians. One of his first patients was an old lady who sent for him and said, "When I was a girl, your grandfather sent me to Cuba to die of tuberculosis. He was gone when I came back, but your father was practising by that time and he looked after me as long as he lived. Now I turn to you to see me through."

Of the cases cited, all except the last, occurred in a shifting, modern city practice, not a favorable field for follow-up data or long acquaintance with patients, which renders the ease with which they were collected all the more striking. So far as prognosis is concerned perhaps we can take a brighter view than we have come to do, when even adults can "outgrow" or compensate defects as marked as these.

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CLINIC OF DR. A. L. LOURIA

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SYPHILIS OF THE LUNG SIMULATING TUBERCULOSIS OR CARCINOMA OF THE LUNG

THE rarity of syphilis of the lung, together with the similarity of syphilis of the lung and commoner pulmonary lesions which it so closely simulates clinically, as illustrated by the case to be presented, warrants the report of this case.

The rarity of pulmonary syphilis, even at the postmortem table, is readily appreciated if one reviews the data of some of the larger series of autopsies, as shown by the following: Symmers, in 4880 autopsies found anatomic evidence of syphilis in 314 cases, with but 12 instances of pulmonary involvement; Osler, in 2800 autopsies at the Johns Hopkins Hospital, 12 cases of pulmonary syphilis, of which 8 were congenital; Lord, among 3000 autopsies at the Massachusetts General Hospital, but one case showing an indurative pneumonitis of luetic origin. In a review of 120 cases carefully selected from the literature, Karshner gives a comprehensive and trite analysis of the pathology and symptomatology of the condition in which he significantly states "Syphilis of the lung is rarely recognized antemortem; in our 55 cases with autopsy, diagnosis was made on the table in 51, but 4 cases being correctly diagnosed previous to autopsy."

Involvement of the upper respiratory tract in the secondary stage of lues, with its usual protracted catarrhal manifestations is too well recognized to require comment here; so too, the occasional occurrence of gummatous formation in the larynx, trachea, or bronchi giving rise to local irritation and resultant cough, which at the time of ulceration is associated with a moderately profuse, mucopurulent, frequently blood-tinged spu-

tum. However, despite the ready knowledge of tertiary visceral lues, its involvement of the lung, giving rise to a clinical entity possible of recognition, is unfortunately either lost sight of or else omitted. Almost thirty years ago, E. G. Janeway called attention to the fact, that with visceral involvement tertiary lues gave rise to irregular fever, night-sweats, and progressive loss of weight and strength, as will be well demonstrated by the following case report.

J. M., male, age forty, married, first seen in June, 1917, giving a history of protracted cough, moderate expectoration, occasional small hemoptysis, afternoon rise of temperature, night-sweats, progressive loss of weight and strength. Previous personal history negative, venereal infection denied by name and symptom.

Physical examination at this time revealed an extensive area of dulness of the right upper lobe, extending downward as far as the level of the fourth rib anteriorly, and to the level of the spine of the scapula posteriorly, the supraclavicular portion of the lung free. Over this area, the voice and breath sounds were somewhat suppressed, bronchial in character, with a moderate number of coarse, moist râles. The rest of the lung bed was essentially negative. Physical examination otherwise not pertinent, no adenopathy, no scar of an initial luetic lesion. Blood Wassermann reaction negative.

Referred for Roentgen investigation, a report was had confirming the physical findings, showing an extensive infiltration of the right upper lobe ("characteristically tuberculous, roentgenologically viewed"). Despite the absence of tubercle bacilli in the sputum on repeated examination, the concurrence of clinical and Roentgen findings warranted the sending of the patient to Lake Saranac. After one month's careful observation and investigation there, the patient was returned home with the final clinical and Roentgen diagnosis of carcinoma of the lung, based on the extent of the lesion, the marked rapid emaciation, absence of tubercle bacilli in oft-repeated sputal examination, and the non-response clinically to usual régime.

Five months later the patient noted multiple painful lumps on

the scalp, at which time he again consulted us. Examination showed these lumps to be definite osseous tumefactions with a sense of central softening; his pulmonary status has been described above. Incision of the multiple tumefactions yielded broken-down, necrotic grumous detritus, which on pathologic examination was reported as a granuloma—no evidence of tuberculosis.

The character of the bony involvement had grossly suggested syphilis as was confirmed by the histologic examination. Blood Wassermann reaction repeated at this time was 4 plus, although negative just previous to operation. The incision into a gummatous mass acting as a provocative has been previously observed by us on several occasions.

In the light of these findings, the patient was put on intensive mixed therapy, a six weeks' course of weekly intravenous injection of old salvarsan with semiweekly, intramuscular injections of soluble mercurial salts, and large doses of iodids orally. The patient made an uneventful recovery, with a relatively rapid disappearance of cough, expectoration, afternoon temperature, and night-sweats. The incised gummata of the skull healing, those not incised disappearing.

Physical examination of the lungs, three months later, showed a slight impairment of the resonance over the above described area of the right upper lobe with a slight diminution of breath, and voice sounds somewhat harsher than normal, no râles. Roentgen investigation, at this time, showed virtually a disappearance of the findings previously noted, with but a moderate increase of the peribronchial markings of the upper right lobe without tendency to agglutination and focal infiltration. The lungs remained clinically negative, and *x*-ray examination in 1922 showed no residual pulmonary infiltration (Fig. 138).

The blood Wassermann reaction remaining positive, the patient was given two more courses of treatment, after which the Wassermann reaction became negative and, routinely taken, remained so.

In March, 1924, the patient developed a very severe bronchopneumonia, the major involvement being that of the right

lung—an area of unresolved pneumonia persisting in the lower portion of the right upper and right middle lobes, with subse-

Fig. 138.—Lungs negative. Aortic arch pronounced. Patient free of pulmonary symptoms. January 7, 1922.

Fig. 139.—Extensive unresolved pnemonia, right upper and middle lobes with beginning cavity formation. July 1, 1924.

quent necrosis and formation of a lung abscess. Repeated examination of the sputum at this time failed to reveal either the presence of tubercle bacilli or Spirochæta pallida. A recurrence

of the symptoms present in 1917, of cough, afternoon temperature, night sweats, emaciation, and the reappearance of a posi-

Fig. 140.—Patient under intensive treatment. Area of gummatous infiltration less. Filbrosis and retraction of right lung becoming pronounced. August 12, 1924.

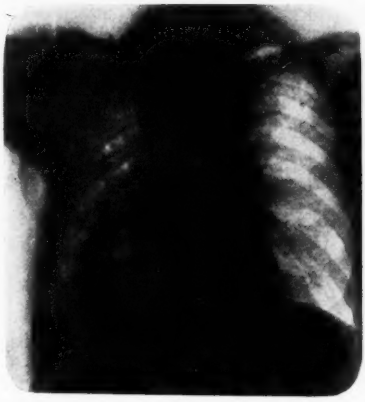

Fig. 141.—Fibrosis and retraction of lung more marked. Residual infiltration slight. The added aortic involvement in Figs. 139–141 as compared with Fig. 138 is marked. Patient free of pulmonary symptoms. This print is reversed. October 1, 1924.

tive Wassermann reaction, warranted further intensive antiluetic therapy. The patient has made an uneventful recovery,

despite the persistence of a positive Wassermann reaction. The right lung has undergone extensive fibrosis and retraction as evidenced on physical examination and confirmed radiographically (Figs. 139–141).

Although lacking a pathological specimen of the lung, the clear-cut clinical progress and reaction to specific therapy seems to warrant the diagnosis of syphilis of the lung; furthermore, the case is of interest in presenting several of the types of pulmonary syphilis as it has been categorically classified: first the pneumonic form mistaken for upper lobe pulmonary tuberculosis, and later carcinoma of the lung, and later the gummatous form, with subsequent necrosis and cavity formation.

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM SIMULATING DIABETES

THE vagaries of syphilis of the central nervous system are spectacularly demonstrated by the following case, a replica of which I have not found in the literature.

A. C., age seventeen, seen in consultation, giving a history of long standing diabetes. One and a half years prior it had been noted that the boy, who was definitely underdeveloped physically, and markedly retarded mentally, began to lose weight, developed an unusual thirst and frequency of urination, together with polyuria, an abnormally voracious appetite (the boy having been previously a very sparse eater), and a brownish pigmentation of the skin, which first appeared on the face and later spread to the extremities and, to a lesser extent, the trunk. Despite intensive dietary régime, the patient failed to respond, showing a persistent although variable glycosuria, ranging from 1 to 6 per cent., blood-sugar from 180 to 260. Previous history, negative. Family history: on subsequent cross-examination, the father admitted having contracted syphilis thirty years ago, for which he was treated in a rather nondescript fashion, the Wassermann reaction having never been taken. Two other children alive and well, revealing no gross luetic stigmata. Mother alive and well, has had no abnormal pregnancies.

Physical Examination.—Emaciated boy who appears to be about fourteen years of age, lying in bed looking chronically ill, anxious, irritable, with a dark, muddy brownish pigmentation of the face, neck, forearms and hands, lower legs, and to a lesser extent the trunk. Eyes prominent, pupils regular, react sluggishly, no extra ocular palsies. Teeth neglected, somewhat irregular in size and shape, slight maxillary prognation, narrow jaw, high arched palate, teeth not characteristically Hutchinsonian in type. Tongue coated, dry; fauces chronically congested, small semi-buried, cryptic tonsils. Neck: small, shotted, dis-

crete glands in both anterior and posterior cervical chains. Chest: symmetrical, poorly developed, expansion normal and equal, lung beds negative except for an occasional squeaking basal râle. Heart: not enlarged nor displaced, regular, forceful and rhythmic, poor muscular tone, no adventitious sounds, rate rapid; blood-pressure, systolic 80, diastolic 30. Abdomen: slightly scaphoid, soft; liver 2 cm. below the costal margin, firm, not tender, surface apparently irregular, abdominal findings otherwise negative. Genitalia fairly developed. Rectal examination negative. Reflexes: marked hyporeflexia. General muscular system poorly developed.

Blood examination showed a slight lymphocytosis, total white count, 8200; polymorphonuclears, 44 per cent.; lymphocytes, 53 per cent.; basophils, 2 per cent.; eosinophils, 1 per cent.; Wassermann reaction negative.

The diabetic syndrome in association with marked pigmentation, enlarged liver, and evident dysendrocrinism had led to the previous diagnosis of hemachromatosis, affording an apparent explanation for the failure of dietary régime. Feeling that a diabetic syndrome may be induced wholly or in part by disease of the central nervous system, as shown by the autoptic cases reported by Brugsch, Lewi and Dresel (4 cases of midbrain sclerosis, with an intractable diabetic syndrome), a lumbar tap was suggested. Clear fluid under marked pressure was obtained, examination of which showed a moderate pleocytosis, 35 cells per cm. all lymphocytes, marked albumin and gobulin rings, a 4 plus Wassermann reaction. Colloidal gold reaction not done.

Under active antiluetic treatment, a very profound impression was made on the clinical course with a disappearance of the glycosuria, the patient being maintained on a restricted diet permitting him 60 gm. of carbohydrates daily. The blood-sugar fell to 150 and persisted there. Concomitantly, the polydypsia and polyuria disappeared, together with a gradual progressive increase in weight and strength. Patient was observed over a period of one and a half years, during which time there was no manifest disappearance of the pigmentation.

Blood Wassermann reaction at first negative, subsequently became positive, and was used in part as index of the persistence of the infection. Further spinal tap was refused by the patient and parents because of the occurrence of semicoma for thirty-six hours succeeded by a persistent headache over a period of four weeks following original spinal puncture, due, I believe, to a gumma of the midbrain, which had given rise to the diabetic syndrome and, following the release of pressure by spinal tap, had been jammed against the base of the skull.

These 2 cases are presented, not alone because of their rarity, but as illustrating both the vagaries of syphilis, and the ability of syphilis to so closely simulate other disease entities as to fail of recognition; in the first instance because of the absence of positive blood Wassermann reaction, and in the second instance because of failure to do a spinal fluid examination in the face of a negative blood Wassermann reaction, recognizing the possibility of the occurrence of a diabetic syndrome on the basis of a central nervous system disease.

CLINIC OF DR. CHARLES SHOOKHOFF

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THE TACHYCARDIAS

THE tachycardias have been chosen for this evening because of their extremely practical importance. The advances, both experimental and clinical, made in the last years, have given us a better insight into their pathogenesis, their classification, their significance, and their treatment.

The term "tachycardia" is used literally and will, therefore, include all forms of rapid heart action. Anything near an exhaustive survey of the subject is impossible in the time allotted, but an attempt will be made at their differentiation at the bedside—graphic and mechanical methods of registration and diagnosis not being stressed. The relationship of the tachycardias to the cardiovascular degenerative diseases will be discussed and methods of treatment will be outlined.

We must not confuse the subjective symptom of palpitation with tachycardia, for while in a great many instances palpitation is one of the symptoms of the tachycardias, it can, of course, be present without a tachycardia.

It will be necessary to briefly review some of the anatomic and physiologic principles underlying the intrinsic and extrinsic cardiac mechanism, to understand the fundamental differences between the various types of tachycardia.

The cardiac impulse takes its origin in the sino-auricular node, a neuromuscular tissue, located in the upper part of the right auricle in the neighborhood of its junction with the superior vena cava. It lies immediately beneath the epicardium. The impulse spreads through the auricular musculature, causing an auricular contraction which, in turn, excites

the atrioventricular node, located in the lower part of the right auricle. From that point the excitation wave is conducted rapidly through the His bundle, which divides at the upper border of the membranous portion of the interventricular septum into the right and left bundle branches, which branches go respectively to the right and left ventricles. These bundle branches spread out into a fine subendocardial Purkinje network, the Perkinje cells making the connection between the specific muscle system and the ventricular musculature. When the excitation wave reaches this point the ventricles become activated to contraction. This briefly represents the normal origin and spread of the excitation and contraction waves.

We are interested in only two of the five properties of cardiac muscle described by Engelmann—rhythmicity and conductivity. Rhythmicity, the ability of heart muscle to initiate its own impulses, is developed to its highest degree in the sino-auricular node. There are lower automatic centers, though, which can take over the pacemakership of the heart when the higher centers fail. The rate—at which these lower centers, *i. e.*, the auriculoventricular node, bundle, bundle-branches, Purkinje system and, finally, the auricular and ventricular muscles are able to generate impulses—diminishes, the lower down in the scale of automaticity they are. Lower automatic centers, when called upon to assume the pacemakership of the heart, will, therefore, do so at a slower cardiac rate. It is important to remember that these very same lower automatic centers may become hyperirritable and, even though the higher centers are not destroyed, the hyperirritable heterotopic focus may take over the pacemakership of the heart at a greatly increased rate, resulting in some of the tachycardias which we will discuss. Conductivity is a cardiac muscle property which is most highly developed in the bundle, bundle branches, and Purkinje system.

Andrus and Carter[1] believe that the cardiac impulse depends upon the loading and unloading of potential differences through a semipermeable cell-membrane, The rate of impulse formation depends upon the relationship of the *p*H in the impulse-building cell and the *p*H of the surrounding tissue fluid. The

permeability of the cell membrane, and through that the differences in potential, is controlled by the CA—K—NA relationship. Increase in the alkalinity of the tissue fluid surrounding the impulse-forming cell increases the potential difference and, thereby, the rate of impulse formation; while increase in acidity has the opposite effect. The oxygen and carbon dioxid relationship affects the heart rate by changing the electrical level within the cell. Haberland[2] has described a specific "sinus hormone" which increases the rate of impulse formation in the sinus node.

The above described succession of events and physiologic phenomena are parts of the intrinsic cardiac mechanism. This mechanism is complete in itself. The isolated heart functions perfectly under proper conditions. It conducts and responds by contraction to impulses which it, itself, originates. The heart is a perfect automatic organ. To make the cardiac output parallel the needs of the organism under varying conditions of rest, exercise, psychic disturbances, etc., we are supplied with what I call a "liaison mechanism," a liaison between the heart and the rest of the body. This mechanism is the extrinsic cardiac system—part of the autonomic nervous system. It is composed of the sympathetic or accelerating nerves, and the vagi or depressing nerves—an antagonistic system. The tone or balance of this system plays an important rôle in the normal, as well as the pathologic physiology of the organism. Through this system the heart receives impulses from the rest of the body—the brain, the intestines, the stomach, the gall-bladder, etc.—and these impulses regulate the normal cardiac response to the needs of the various organs separately, and the body as a whole. Any imbalance of this system may cause abnormal cardiac rates. It should be remembered that the extra cardiac nervous mechanism has its greatest control over the sinus because of its direct nerve supply through the sino-auricular ganglia, and the lower automatic centers are further and further removed from its control.

The normal heart rate in adults is between 70 and 80 beats per minute, and is influenced by the rate of impulse formation

in the sinus node and the tone of the extracardiac nervous mechanism. The heart rate can be changed either by the loss or disturbance of function of the sinus node, or by hyperirritability of the lower automatic centers. Changes in oxygen, carbon dioxid balance in the cell, changes in the *p*H in the cell or outside of the cell, changes in potassium, calcium, and sodium balance, changes in temperature, all affect the rate of impulse formation in the sinus. Changes in the tone of the extracardiac nervous mechanism affecting the sinus node or the lower centers, will disturb the rate by increasing impulse formation in the sinus, or by producing single ectopic beats or a series of such beats.

CLASSIFICATION OF THE TACHYCARDIAS

1. Sinus, or nomotopic tachycardias—those arising in the sinus.

2. Heterotopic—those arising from foci other than the normal pacemaker.

SINUS TACHYCARDIA

In these tachycardias the sinus is still the pacemaker. They are a simple exaggeration of a normal phenomenon, caused directly by an overirritable or an overirritated sinus node, or indirectly by a disturbed vagus or sympathetic balance.

Excitement, exercise, etc., increase the cardiac rate. The needs of other organs distant from the heart will, by reflex impulses through the extrinsic mechanism, increase or decrease the cardiac rate to suit the needs of those organs. It is only when the response to such impulses is in its severity and duration out of proportion to the intensity of the exciting factor that such tachycardias are pathologic.

Examples of sinus tachycardias are: those caused by coffee by its direct action upon the sinus (Cushny[3]); alcohol, by reflexes from the mucous membrane of the mouth and the stomach (Dixon[4]); nicotin, both by its direct action upon the cardiac musculature (Wertheimer[5]), and by paralysis of the ganglia of the autonomic nervous system in the heart (Clerc and Pezzi[6]).

Any toxic focus or toxic disease may be the cause of increased sinus activity. A common example is the tuberculotoxic tachycardia, which may be the very earliest symptom of an active incipient tuberculosis.

Tachycardias in endocrine secretory disturbances are common. In thyrotoxicosis it is presumed that the increased or altered thyroid secretion causes an increased sensitization of the sympathetic system to the adrenalin already present in the blood. In the latter stages of thyrotoxicosis the tachycardia may be due to myocardial degeneration. Cannon and Smith[7] believe that the thyroid secretion has a direct effect upon the heart muscle itself. The tachycardias of the menopause and following castration are also of this type.

In febrile diseases sinus tachycardias are caused by the effect on the sinus of the increased temperature, or the effect of the toxemia of the disease, or both. The same factors, in addition to disturbances caused by local pathology, pertain in the infectious diseases of the heart itself. The only symptoms of a fresh or a superimposed endocarditis may be an increase in the cardiac rate.

In the anemias, the increased rate is probably due to the diminished hemoglobin content of the red blood-cells, and in the later stages to the myocardial degeneration.

Any diseases like pleuropericardial adhesions, mediastinitis, mediastinal new-growths, either malignant or benign, may by involving the vagus cause tachycardias.

One must not overlook old myocardial infections or degenerations as a possible cause of a simple tachycardia that may be thought to be of nervous origin. A common example of this is the so-called postinfluenzal, cardiovascular, functional disorder which is really a myocardial degeneration. Constitutional cardiac inferiority, like hypoplasia of the aorta or hypoplasia of the heart itself, must be ruled out before we can accept cardiac neurosis as a cause of a sinus tachycardia.

Sinus tachycardias are always gradual in their onset and gradual in their ending. In most cases the rate is between 90 and 120, although rates as high as 180 beats per minute do

not necessarily rule out a tachycardia of sinus origin. Rates above these figures seldom arise in the normal pacemaker.

The sinus reactions described by Winterberg[8] are extremely useful in the differential diagnosis of the tachycardias. These reactions are: 1. Respiratory. 2. Postural. 3. Carotid sheath or oculobulbar pressure. 4. Exercise.

If we find an increase in rate on deep inspiration and a slowing on expiration, a changing rate with change of posture, or a slowing of the rate caused by oculobulbar or carotid sheath pressure, or gradual changes in the rate with exercise, we can be sure we are dealing with a sinus tachycardia. The absence of these reactions, however, does not rule out a sinus tachycardia, for we know that, in the higher cardiac rates, respiratory postural or reflex vagus effects are often absent.

The exercise test because of its simplicity is the best. A gradual increase during, and a gradual decrease following exercise is the best indication of a sinus rhythm. If the rate changes in proportion to the amount of exercise, the increased sinus rate is physiologic, but if the response, in its rate and duration, is out of proportion to the amount of exercise, it is pathologic. Only severe exercise can cause slight changes in the rate of the heterotopic tachycardias. In some cases the differential diagnosis will be made only by electrocardiographic or polygraphic studies.

Treatment.—The treatment of sinus tachycardias depends upon the cause. Forbidding of coffee, tea, nicotin, or alcohol if they are the exciting factors, treatment of the cardiac decompensation, the thyrotoxicosis, the anemia, etc. is indicated. If, after a febrile disease, the tachycardia does not subside with the subsidence of the rest of the symptoms, one must suspect damage to the endocardium, myocardium, or pericardium. In the neuroses, hydrotherapy, change in climate, and psychotherapeutic measures are of value. Bromids or quinin in small doses may be used to reduce the increased cardiac irritability.

The **prognosis** of these tachycardias is dependent upon the prognosis of the underlying disease.

HETEROTOPIC TACHYCARDIAS

The heterotopic tachycardias are those having their place of origin other than in the sinus node. They are divided into:

1. Paroxysmal tachycardias.
2. Auricular flutter.
3. Auricular fibrillation.

The **paroxysmal tachycardias** are characterized by the sudden onset of a series of responses of the cardiac muscle to impulses, arising at a high rate of speed from a single irritable focus other than the normal pacemaker. They are (1) auricular, (2) nodal, (3) ventricular, depending upon the location of the ectopic pacemaker.

While the auricular paroxysmal tachycardia, which is the most common form, may occasionally be clinically differentiated from the other two by its behavior to vagal stimulation and by its absolute regularity, the ventricular type having occasionally some irregularities in rate, graphic methods must, as a rule, be used for their differential diagnosis.

Paroxysmal tachycardias may occur at any age. Colgate and McCulloch[9] report a case in an infant twenty-four days old, and another case in a child three weeks old. They found no evidence of cardiac disease between attacks. Schuster and Patterson[10] have reported cases in children, respectively nine weeks and four days old. Both these children died, and at autopsy congenital cardiac defects were found. They occur in young people with or without pre-existing cardiac disease. During the interval between the paroxysms extrasystoles may occur, and are usually of the same form as those of the paroxysm. In older individuals, unless they give a history of having previously had extrasystoles or attacks of tachycardia, their onset is indicative of severe myocardial damage. All types of paroxysmal tachycardia are characterized by a very abrupt onset and an equally abrupt ending. They start at full rate, and end with a sudden resumption of the normal sinus rhythm. The length of the attacks may vary in the same individual from a few seconds to hours and days. The cardiac rates may be between 150 and 250 beats per minute. Rates above 250 are

uncommon. The most usual rate is between 180 and 200 beats per minute. As a rule, there are no variations in rate in the paroxysm, and the sinus reactions are absent.

The bedside picture varies with the length and degree of the tachycardia, as well as the previous condition of the heart itself, hyposensitive individuals may give no symptoms. Mild attacks may cause very little discomfort. In severer attacks there may be palpitation, throbbing of the head, faintness, dizziness, exhaustion, and even a sense of impending death. Ventricular tachycardias not infrequently end in ventricular fibrillation and death.

The symptomatology is dependent upon which side of the heart bears the brunt of the attack. Most commonly, as the attack continues, all the definite signs of a right-sided heart-failure appear, due to failure of the lesser circulation, continual dyspnea, cyanosis, marked throbbing of the superficial cervical veins, râles at the bases of the lungs, a large and tender liver, which in turn may cause severe abdominal symptoms such as vomiting, distension, abdominal pain, and other signs which may be mistaken for evidence of a surgical condition will appear. All grades of edema, from slight pitting of the dependent portions of the body to a general anasarca, may be seen. Due to the failure of the greater circulation caused by the diminution in left ventricular output, all varieties of cerebral symptomatology, spontaneous dyspneas, Cheyne-Stokes respiration, cardiac psychoses, cardiac asthma, Stokes-Adams-like picture, convulsions, epileptiform seizures, etc. may be encountered.

Barnes[11] has recently pointed out the importance and frequency of cerebral symptomatology in the paroxysmal tachycardias. The ventricular type seem to give the more severe signs of cardiac failure and particularly failure of the greater circulatory type, probably because they are more common in patients with pre-existing myocardial disease, and because of the abnormal spread of the excitation wave. In these cases the pulse may show alternation during or shortly following the attack.

The arterial pressure falls, because of the marked shortening of the diastole and the consequent insufficient rest and

recovery time and insufficient ventricular filling. Frequently, because of the simultaneous contraction of the auricle and the ventricle causing the auricle to contract against closed auriculo-ventricular valves, there is an insufficient ventricular filling (Wenckebach)[12]. In the ventricular tachycardias, the abnormal character of the ventricular beat causes a lessened systolic output. Any insufficiency in ventricular output may cause an insufficient coronary circulation, and this in turn will cause further myocardial weakness.

The size of the heart during the attack is of interest. Wenckebach[13] has reported a decrease in size. Vaughn[14] has reported a 1 cm. increase in one case, and Wilson[15] a $2\frac{1}{2}$ cm. increase in another case. The writer has recently seen a case at the cardiac clinic of the Brooklyn Jewish Hospital, a male adult whose teleoroentgenogram, taken in an attack of auricular paroxysmal tachycardia that had already lasted eight hours, showed a definite increase of 1 cm. in the diagonal diameter over a 6 ft. plate taken one hour after the attack had subsided. In the interval between paroxysms in this case no evidence of cardiac disease could be found.

The attacks end as suddenly as they begin, and usually, particularly in those cases in which no cardiac disease had previously been found, the signs of cardiac embarrassment disappear almost immediately. A waterlogged patient may in a few hours be completely compensated and at work.

There are no characteristic anatomic pathologic changes. There may be no anatomic pathology. The attacks may be only functional. Excitement, worry, etc., in persons with a labile extracardiac nervous mechanism, may be the only causative factors. The postpartum tachycardias may be of this type. Some postpartum and postoperative cases may be due to the effect of the anesthesia, either directly on the heart-muscle, as in chloroform anesthesia, or by its effect upon the tone of the extracardiac nervous mechanism. The handling and stretching of the peritoneum and other tissues may initiate postoperative attacks. Toxic foci, tonsils, gall-bladder, etc., are frequently causes and should be looked for in unexplained cases.

In one patient seen by the author, an incipient tuberculosis was the only possible explanation for attacks of auricular paroxysmal tachycardia.

Frequently chronic endocardial diseases, which by their disturbed mechanics cause dilatation of the cardiac chambers, may, due to the stretching of the chamber wall, be a factor in the causation of either extrasystoles or paroxysmal tachycardia.

Pathologic processes involving the vagus may cause attacks. Graber[16] reports a case of Hodgkin's disease, in which the right and left vagi were involved by pressure of enlarged mediastinal glands, causing attacks of auricular paroxysmal tachycardia.

Of importance is the relationship of the cardiovascular degenerative diseases to the paroxysmal tachycardias. Lewis,[17] Smith,[18] Scott,[19] and others, by ligating various branches of the coronary vessels have caused ventricular extrasystoles, paroxysms of ventricular tachycardia, and ventricular fibrillation.

The anatomic pathology, when found, is in the greater number of cases dependent upon changes in the cardiac muscle, due to closure by embolism or thrombosis of coronary branches and the consequent muscle infarction. Robinson and Herman,[20] and others have reported fibrotic infarctive changes due to coronary occlusion. Willius and Barnes,[21] in an analysis of a series of cases, found 44 without disease, 35 with cardiovascular degenerative disease due to hypertension, arteriosclerosis, lues, or chronic nephritis, and 24 due to Graves' disease or toxic adenoma of the thyroid. Lesions in the neighborhood of the sinus node have been found by Butterfield[22] in 2 cases of supraventricular tachycardia. Neither in site, nor in character are the lesions specific. It is generally believed that the ventricular paroxysmal tachycardia is more frequently associated with cardiovascular degenerative disease than the other types, and the onset of an attack may be the only symptom of a coronary closure.

Treatment.—In the attack our efforts should be directed to the diminution in this number of ventricular contractions, if possible, by depression of the irritability of the ectopic focus, and the re-establishment of the sinus pacemaker.

Many patients, particularly those who suffer with the functional types, have for themselves learned various methods, such as deep breathing, holding the breath, changing position, yawning, vomiting, etc., to stop their attacks. These methods depend upon vagal stimulation for their efficacy, and are, as a rule, only successful at the beginning of the attack.

Carotid-sheath or oculobulbar pressure have, by reflexly stimulating the vagus, been successful in ending attacks.

All methods depending upon vagal stimulation are effective only in the auricular types. This fact may be used as a clinical means for differentiating them from the ventricular or nodal tachycardias.

The intravenous use of digitalis and strophanthin, particularly in those cases where the tachycardia is due to disease of the myocardium, often gives good results. Levine and Blotner,[23] Otto and Gold,[24] and others have reported cases of all types in which all other methods had failed, and complete digitalization kept the patient free from attacks. The effect of digitalis depends upon its action in causing a slowing in rate, a lengthening of the diastole, a strengthened systole, and thereby an improvement in the coronary circulation. This improved blood-supply may remove the cause of the irritability of the ectopic focus. It thus may re-establish the sinus as the pacemaker. In the auricular forms, the effect of digitalis is dependent upon vagal stimulation.

It might be well at this point to mention one of the most frequent dangers of digitalis therapy in severe myocardial disease. Gilchrist,[25] Danielopolu,[26] Eggleston and Wyckoff,[27] Felberbaum,[28] Reid,[29] and Resnick[30] have reported cases of paroxysmal tachycardia resulting from digitalis used in the treatment of severe myocardial degeneration. It is thought that patients, in whom myocardial degeneration is far advanced and in whom the degree of heart-failure is steadily increasing, become more susceptible to the direct action of the drug upon the heart-muscle. It is well to remember, therefore, that in a patient with advancing cardiac failure and under treatment with digitalis, the occurrence of a paroxysmal tachycardia is of the most serious conse-

quence. One will usually be forewarned of such an occurrence by the appearance of extrasystoles.

In recent years, quinin and quinidin have been successfully used in the treatment of the paroxysmal tachycardias. Winterberg,[8] who first used quinin intravenously in these conditions, has had very good results. The writer has seen excellent results from 7½ gr. of quinin bisulphate given intravenously. The attack often ends before the needle is withdrawn. Sterile water, intravenously, has been given to rule out the possible psychic effect of the introduction of the needle. In some cases it takes a few minutes before the attack ends. Failure in obtaining results may be due to insufficient dosage. Winterberg has given as much as 15 gr. intravenously each day. Such doses are rather high. In a patient who has shown no signs of cinchonism, an increase in the dosage is justified. It must always be remembered, however, that quinin is a protoplasmic poison, and one must be careful in its use, particularly in cases of severe myocardial damage. In some patients, the effect of the drug, repeatedly used, diminishes, the time of response lengthens, and increased dosage is necessary to get results.

The intravenous use of quinin is justified only in severe attacks. In the milder cases, the peroral administration will frequently control attacks and sometimes prevent their recurrence. Any evidence of cinchonism is a contraindication to the use of the drug.

The action of quinin is dependent for its effect upon its depressant action on all cardiac properties, and particularly upon the property of irritability.

Recently Von Stepp and Schliephake[31] have reported favorable results in cases treated with cholin. It is dependent for its results upon its marked vagal stimulant action. It might be tried in those cases in which quinin is contraindicated.

In between paroxysms, attempts to determine the basic cause, and efforts to remove that cause should be made. Hoffman[32] has found that young people with the functional types may be relieved of attacks in altitudes of 1500 to 1800 meters.

Calcium chlorid, physostigmin, and ovarian therapy all have been used, with varying results.

The *prognosis* of the paroxysmal tachycardias depends upon whether they occur in patients with or without organic heart disease. Very *rarely* a functional case may succumb due to our inability to stop the attack. As a rule, the attacks may last even for weeks without any grave danger. The prognosis of the pathologic types is dependent upon the severity of the underlying pathologic conditions. Functional types arising in patients with previously damaged hearts are more serious, naturally, than those of the purely functional types. When the onset of the paroxysmal tachycardia is a symptom of coronary closure, the prognosis is grave. As had already been mentioned the ventricular types are of severer prognostic moment.

Auricular flutter is also a tachycardia of ectopic origin. It is similar in a sense to the auricular paroxysmal tachycardia. In the latter condition, there is an irritable focus somewhere in the auricle which causes the production of auricular contractions at about 200 contractions per minute, each auricular contraction being followed by a ventricular contraction. In auricular flutter, instead of one single focus there is an irritable ring usually located in the upper part of the auricle, through which an impulse is continuously traveling at the rate of about 300 circuits per minute, and from which the auricular musculature gets its excitatory impulses. The auricle, therefore, contracts approximately 300 times per minute. This large number of impulses is too much for the conduction system and a functional block is the result. The degree of the functional auriculoventricular block determines the ventricular rate.

Only every second, third, or fourth auricular impulse may be conducted to the ventricles and pulse rates of 150, 100, or 75 per minute result. In a patient with a pulse rate of 75 flutter may not be suspected, for auscultation and palpation will reveal no abnormalities. The most usual ventricular rate in flutter is 150, and is caused by a 2 to 1 A-V block. At such a rate flutter simulates a sinus tachycardia. The sinus reactions though are absent.

Due to the functional block in flutter, and due to the improvement of conduction caused by sympathetic stimulation, exercise, which stimulates the sympathetic, gives us a means of diagnosing flutter clinically. Exercise in a patient with a ventricular rate of 75 may suddenly increase the rate to 150, 225, or 300, depending upon the previously existing degree of block, and the degree of improvement of the block by the sympathetic effect of the exercise. A 4 to 1 block may be changed to 3 to 1, 2 to 1, or to no block, every auricular impulse being conducted. Upon the recession of the effects of the exercise the rates suddenly return to their previous level. This reaction is not always present, but when it is, it is absolutely diagnostic of auricular flutter. After severe exercise a flutter with a regular rate may become irregular, due to changing A-V block. This is also diagnostic of flutter. Occasionally a patient may have a flutter with an irregular rate, and exercise may make it regular.

Patients with flutter and a slow ventricular rate may have attacks simulating attacks of paroxysmal tachycardia. These attacks are caused by sudden sympathetic stimulation or vagal depression. Their onset and ending are abrupt. The sinus reaction will differentiate them from the paroxysmal tachycardias.

The reaction to exercise in flutter is not caused by an increased impulse formation in the sinus, it is not a sinus reaction. The doubling or quadrupling of the rate and the suddenness of the rate changes speak against that. There is absent the gradual increase in rate and the relationship of the increase to the amount of exercise that is so characteristic of the sinus reactions.

When these above described reactions to exercise are not present only graphic methods of diagnosis are of avail.

The pathology and treatment of flutter will be discussed together with the pathology and treatment of auricular fibrillation.

Auricular fibrillation is closely allied to auricular flutter. It also has its pathologico-physiologic basis, an irritable ring in the upper part of the right auricle, around the mouth of the superior vena cava, through which an excitation wave is traveling, but at a rate so high—400 to 600 circuits per minute—that the auricle

is unable to respond with co-ordinated contractions. Because of this inco-ordination of contraction of the auricular musculature, there is no propulsion of blood to the ventricle. There is no auricular systole. Impulses of varying intensity and at great irregularity are being transmitted to the ventricle, which responds by an absolute irregularity in rate and force of its systoles.

In auricular fibrillation, as in flutter, the degree of functional A-V block influences both the clinical picture and the treatment. The greater the block, the slower the ventricular rate. A complete irregularity of cardiac action both in rate and force of ventricular contractions, with a complete absence of a basic rhythm, is auricular fibrillation. The rapidity of the ventricular rate determines the degree of cardiac decompensation.

In mitral stenosis, the presence of an auricular fibrillation causes the rough crescendo presystolic murmur to be replaced by a long diastolic decrescendo murmur. A complete irregularity with a ventricular rate of 120 or over is most usually auricular fibrillation.

Auricular fibrillation and flutter may occur in any of the chronic endocardial diseases, whether rheumatic, luetic, or arteriosclerotic. It is most frequently found in mitral stenosis. It is a very common symptom of the myocardial degeneration in the thyrotoxicoses, and thyrotoxicosis should always be looked for in all cases of paroxysmal auricular fibrillation. It is often present in both the essential and secondary types of greater circulatory hypertension. Weber has reported cases occurring in young men without previous cardiac disease who had undergone severe psychic strain. Coronary closure may manifest itself only by the sudden appearance of an auricular fibrillation. It occurs in other forms of myocardial degeneration. Digitalis may induce auricular fibrillation in cases of cardiac decompensation with slow heart rates (Mackenzie[33]).

Treatment.—The treatment of these conditions may be divided into: (1) The treatment of symptoms, (2) attempt at re-establishment of the normal cardiac mechanism.

The symptomatology, as stated above, is dependent upon the degree of A-V block, and in digitalis we have a means for in-

creasing that block and reducing the number of ventricular contractions, and increasing the cardiac output by giving the heart a longer diastole and a better filling. Digitalis must be used in amounts sufficient to obtain the required results. The occurrence of nausea, when due to the action of digitalis locally upon the gastric mucous membrane, should make it necessary for the digitalis to be given intravenously, subcutaneously, or rectally.

Extrasystoles arising in the course of digitalis therapy should be sufficient reason for discontinuing treatment. Occasionally ventricular fibrillation will occur in such cases (McWilliams[34]).

When the desired result from digitalization is obtained, a maintenance dose must be decided upon, and this may be given for long periods of time.

Digitalization often causes flutter to go over into auricular fibrillation. The digitalis is then stopped, and the sinus may resume its normal function. If the fibrillation persists, small doses of quinidin may be given to re-establish the normal pacemaker.

It must be understood that auricular fibrillation *per se* with a normal ventricular rate is no indication for the use of digitalis, unless the underlying cardiac condition is the cause of the decompensation.

Overdosage of digitalis may cause so marked a degree of A-V block that a Stokes-Adams syndrome may occur.

It is to be remembered that a nurses' chart of the pulse rate is no indication for or against the continuance of digitalis therapy. The greater the ventricular rate the slower the radial pulse may be, due to a greater pulse deficit. Always count the apical impulses for ventricular-rate indications for digitalis therapy.

The attempt to re-establish a sinus rhythm in cases of auricular fibrillation by the use of quinidin or quinin should be made only in those cases where the attacks are paroxysmal, and where between attacks there are no evidence of severe cardiac disease. In such cases, if the attack is severe, even intravenous quinin therapy, as employed in the paroxysmal tachycardias may be used. The use of quinidin may also possibly be justified in cases in which the fibrillation has not been

of long duration, and where there are no signs of myocardial weakness. On the whole, however, the writer is not in favor of the use of quinidin in an attempt to establish a sinus pacemaker for the following reasons:

1. Even a successfully re-established pacemaker is sooner than later replaced by the heterotopic focus.

2. The underlying factor that has caused the auricular fibrillation has, in most cases, not been removed.

3. Quinidin, as has been previously stated, is a severe protoplasmic poison, and its effect on an already severely damaged myocardium is, whenever possible, to be avoided.

4. A proper ventricular rate alone is necessary for the patient's well being. The fibrillation of the auricle in itself, except in hypersensitive persons, may cause no disagreeable symptoms.

Occasionally in auricular flutter, after the use of quinidin, the ventricular rate will suddenly rise to 200 or over. Quinidin depresses conductivity, increases the refractory period of the cardiac muscle, and will, in some cases, cause only a slowing of the circuit rate without completely destroying the circuit movement. This slowing of the circuit rate causes a decrease in the number of impulses sent to the bundle to be conducted to the ventricle. Due to the decrease in the number of auricular impulses, the conductivity of the bundle is functionally improved and it may then be able to conduct every impulse, with a consequent sudden marked increase in the ventricular rate. This event, occurring in a patient with a damaged myocardium, may cause symptoms of severe decompensation.

CONCLUSIONS

In conclusion a short résumé of the clinical differential diagnostic points in the various types of tachycardia is outlined:

1. The rate in physiologic sinus tachycardia increases gradually and decreases gradually in direct proportion to the amount of exercise.

2. The rate in pathologic sinus tachycardia gradually increases and gradually decreases, and in its severity and duration is out of all proportion to the amount of exercise.

3. All sinus tachycardias respond to some or all of the sinus reactions described by Winterberg.

4. The rate of sinus tachycardias rarely exceed 160 beats per minute.

5. The onset of paroxysmal tachycardias is always abrupt, and the ending is always abrupt.

6. The sinus reactions do not influence the rate of paroxysmal tachycardias. Vagal stimulation may suddenly stop an attack or initiate one.

7. Vagal stimulation does not effect the ventricular paroxysmal tachycardias, and they are at times slightly irregular.

8. The most usual rate in paroxysmal tachycardia is between 180 to 200 beats per minute.

9. The doubling or quadrupling of a rate by exercise makes the diagnosis of flutter certain.

10. When strenuous exercise causes an irregularity in a person with a regular pulse, flutter with changing A-V block must be ruled out. The most usual rate in flutter is 150 beats per minute.

11. An irregularity which is present with a cardiac rate above 120, and which increases on exercise, is most usually auricular fibrillation.

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BRONCHOSCOPY IN THE TREATMENT OF LUNG SUPPURATION

A SUPPURATIVE process in the lung which causes the patient to cough frequently and expectorate a large quantity of exudate, which may be foul-smelling, is a matter of serious concern to the individual and his attending physician. If left untreated, a majority of these patients have a limited duration of life. While they live, their pulmonary condition prevents their enjoyment of many of the pleasures of life. A better knowledge and understanding of the causation, the clinical behavior, and the treatment of these conditions, together with their ultimate outcome under different circumstances of care and supervision, is important.

All lung suppurations begin as acute processes. They may originate as the result of aspiration of septic material during operations, the aspiration of foreign bodies which are permitted to remain in the bronchial tree, the delayed resolution of a pneumonic process, or as the result of an embolic process from the site of operation or from an infected wound. There also exists such a condition as a dry bronchiectatic process, upon which there may be superimposed an acute infection. We have also seen a patient develop lung suppuration as a result of the overflow from an obstructed esophagus due to lye stricture, and another patient suffer similarly because of the aspiration of part of the contents of a pulsion diverticulum of the esophagus. A majority of the operations which are complicated by lung suppuration are performed upon structures of the respiratory tract, particularly the tonsil. In a bronchoscopic study of 200 anesthetized tonsillectomy patients, the writer found that 155

had the tonsillectomy blood mixture in varying quantity in their trachea and bronchi.

The presence of suppurative sinus disease has been found to have an etiologic significance in these lesions. The sinus infection will also interfere with the proper healing and cure of the pulmonary condition.

Acute lung suppuration is readily recognized, once the patient begins to expectorate a foul-smelling sputum, or a foul odor of the breath is noted where before there was none present. Until this time the condition simulates a localized pneumonia, and is considered as such. The patient may have pain in the chest corresponding to the site of the lesion, his temperature is elevated between 99° and 104° F., and at times higher. There is profuse expectoration and spasmodic cough, recurring at frequent intervals. The patient perspires, his appetite is poor, and he is quite sick.

Physical signs will vary according to the location of the involved area and its state of fulness or emptiness with exudate. The size of the area will matter. Perhaps the most constant findings in lung suppuration of the acute type are those associated with impaired respiratory movement and the interference with the transmission of breath-sounds.

Treatment.—A fair proportion of acute lung suppurations will recover spontaneously; perhaps 40 per cent. There is, however, no way of telling which case will recover spontaneously. Bronchoscopy offers a rational form of treatment with a promise of 90 per cent. of cures in this type of case. This statement is based upon personal experience and the many cures which many well-known bronchoscopists are securing in their daily practice. The expectant or medical treatment amounts to a policy of waiting to see whether the patient will recover spontaneously or whether he will go on to a subacute or chronic form of illness. A majority of these suppurations are of the bronchiectatic variety rather than of the single abscess cavity type. What governs the production of the one or the other is not entirely understood.

The local conditions in the involved area are such as to favor

the use of bronchoscopy. It is not only the pneumonitis around the suppurative area, but also the excess of exudate which is retained that produces the toxemia. This is so because the patient is unable to expel the accumulated products of the local infection. The cilia are impaired, and the bronchial musculature is either thinned out or thickened by the local reaction, so that proper contracture and peristalsis are interfered with. In addition, the lack of proper resiliency and elasticity in the involved area prevents the extrusion of its abnormal contents. The patient's expulsive effort is interfered with because of pain and weakness.

In the hands of one sufficiently skilled, the bronchoscope overcomes the loss of these essential factors of expulsion. The bronchoscopist can at once see the bronchial branch which is nearest to the field of suppuration, and attack it by means of his aspirating or irrigating tube. Very frequently the thorough evacuation and cleansing of the involved area will be sufficient to permit Nature to bring about a cure. Any procedure that will remove the active infection and evacuate the retained accumulated exudate, so that Nature may cause a collapse and obliteration of the cavity or a return to normal of the dilated bronchial branches, will cause a cure. Therefore, bronchoscopy is particularly suited to this condition.

These lesions should be treated as early as is possible. For this same reason, aspirated, foreign bodies whose continued presence usually causes lung suppuration, should be removed from the bronchi at once or as early as possible, even in the presence of acute symptoms. As was stated before, fully 90 per cent. of acute suppurations of the lung are curable by bronchoscopy. The reason that all are not curable lies in the fact that unfortunately there occasionally occurs a fulminating type of infection which does not respond to any form of treatment. Then there is the type of suppuration which after several bronchoscopic treatments does not result in a cure, although there may be marked improvement. This lack of favorable response to treatment can frequently be traced to the presence of a nasal sinus infection, which may be readily recognized or may be latent.

The following are examples of acute lung suppurations which were successfully treated with the bronchoscope.

Case I.—J. E., a man, age forty, had his tonsils removed under local anesthesia in June of this year. Ten days later he was admitted to the service of Dr. Blatteis because of fever, cough, and foul expectoration. He also experienced pain in his left chest which was more severe in the evening. Examination

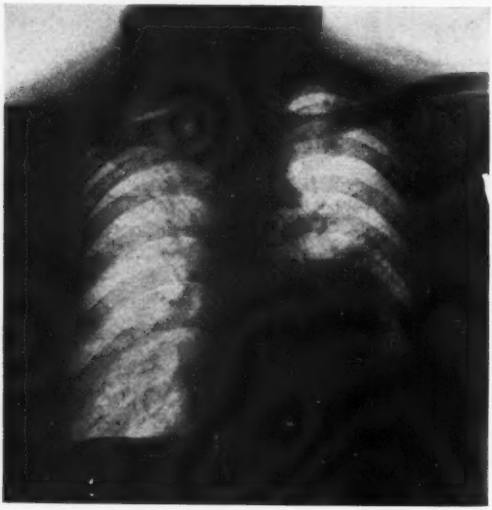

Fig. 142.—Case I. Lung suppuration following tonsillectomy. Left lower lobe —multiple bronchiectatic processes. Recovery after two bronchoscopies.

revealed a decreased resonance at the left base. The Roentgen film showed a shadow in the lower half of the left lung field. The patient was referred for bronchoscopy on the twenty-first day of his illness. The left lower-lobe bronchus was found to be markedly dilated, as were also the main bronchial branches. Pus was seen to be coming from a posterior and inferior branch with each expiratory effort, after the main bronchus and its branches were emptied of their content by aspiration. On the day following the bronchoscopy, the sputum had decreased from

16 ounces a day to 7 ounces a day. His temperature gradually came down to normal, although it was as high as 103° F. on the afternoon preceding the day of bronchoscopy. Ten days later he expectorated but 1 ounce a day. He was again bronchoscoped at this time. It was found that the dilatations had almost entirely disappeared. Within forty-eight hours after his second bronchoscopy the expectoration had entirely ceased, and the patient was considered as recovered. Whereas study of the expectoration

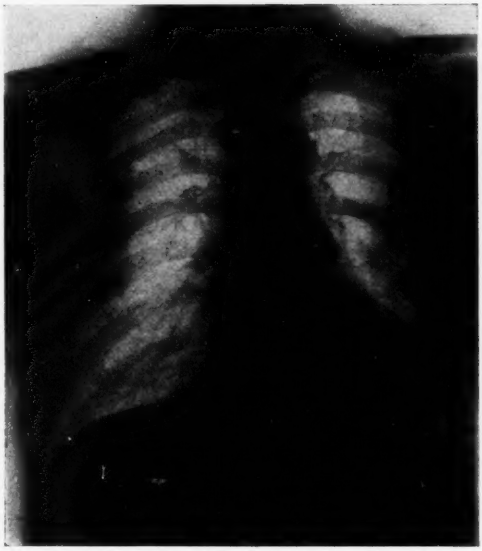

Fig. 143.—Same patient as Fig. 142, two months after last bronchoscopy.

yielded a large variety of organisms, the specimen removed through the bronchoscope yielded a pure culture of non-hemolytic streptococcus. The accompanying roentgenograms show the condition before and shortly after bronchoscopic treatment. A very definite clearing of the involved area is to be seen on the second film (Figs. 142, 143).

Case II.—W. M., a man, age thirty-two, had received several doses of neosalvarsan intravenously. Shortly after his last

dose he experienced pain in his right chest, had fever, and expectorated a large quantity of foul-smelling sputum. The patient was seen by Dr. M. A. Rabinowitz, who referred him for bronchoscopic treatment. Bronchoscopy was performed during the second week of the patient's illness. At bronchoscopy the right

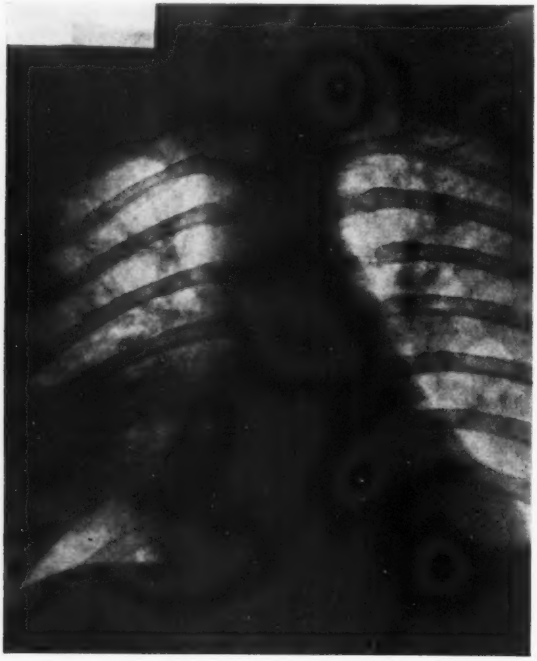

Fig. 144.—Case II. Acute suppuration right lower lobe—localized abscess type. Recovery after one bronchoscopic treatment.

lower-lobe bronchus and its visible branches were found to be dilated. Pus was seen to be coming from a mesial branch with each expiratory effort. A single bronchoscopic irrigation, after the technic first used by Yankauer, was sufficient to bring the temperature down to normal within twenty-four hours. The expectoration ceased entirely within four days, and the patient

was considered as recovered. He has been free from symptoms for more than a year (Figs. 144, 145).

It is the chronic suppurative lesions of the lung which are less responsive and more perplexing to handle. In this type of case, the suppurations following foreign-body aspiration are the most favorable in their final outcome. For in these cases where the foreign body has not been lodged too long, and where permanent local changes have not taken place, the simple bronchoscopic removal of the foreign body will frequently be followed by

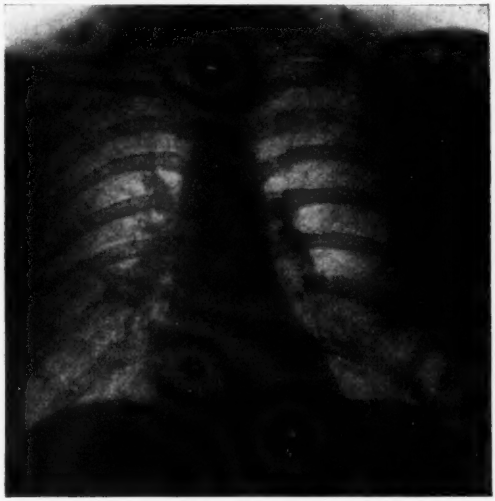

Fig. 145.—Case II. Same patient as Fig. 144, ten months after treatment.

complete recovery. A metallic foreign body, such as a straight pin or a bar-pin, may lodge in a branch bronchus for many years without causing symptoms. Or the local changes following the aspiration of a metallic foreign body may be so slight as to be compatible with a cure. But foreign bodies which are of organic composition, such as bones or nut shells, will usually cause lasting suppuration unless they are removed early. Once there is fibrosis and fixation of the bronchial and peribronchial structures, it is difficult to conceive of cure by bronchoscopy.

Experience has shown that the patient with a chronic suppurative lesion can be improved and made fairly comfortable for a limited period of time. This period is usually one day to one week. Weekly irrigations through the bronchoscope will keep some of these patients comfortable, will cause a disappearance of the clubbing of the fingers and toes, the cough will be lessened in frequency, the expectoration lessened in quantity, and the odor, if one is present, will disappear from the sputum. When it is not practical to carry out this form of treatment, some other type of treatment will have to be considered. The patient who is benefited for but one or two days is obviously in need of something better than bronchoscopy if such a thing is at hand. It is therefore of great advantage to these sufferers that the surgeon and the internist be consulted by the bronchoscopist in outlining the best type of treatment for such a case. Certain types of these chronic cases lend themselves admirably to surgical procedures. These, after consideration and consultation, should be referred to the surgeon. On the other hand, there are some cases which, because of the extent or multiplicity of their involvement, will not be helped much by any form of therapy.

Case III.—This is a case of chronic lung suppuration which followed the aspiration of a fragment of beef bone. M. G., a man, age twenty-one, was referred by Dr. M. Fishberg for bronchoscopy, because he suspected the presence of a foreign body in the left lower lobe of the lung. During a period of three and one half years this patient had been to several physicians. He had been tested and treated for asthma, tuberculosis, and lung suppuration, and had been sent far from home in search of relief from his suffering. Despite the fact that his symptoms dated from the time that he had choked while drinking soup three and one half years before, no attention had been paid to the possibility of his having aspirated a foreign body. Dr. Fishberg could not correlate the findings in the left lower lobe and clear apices with a diagnosis of tuberculosis. He suspected the presence of a foreign body, and referred the patient for bronchoscopy.

At bronchoscopy the left lower-lobe bronchus was found to be filled with pus. Upon the withdrawal of the pus, granulations,

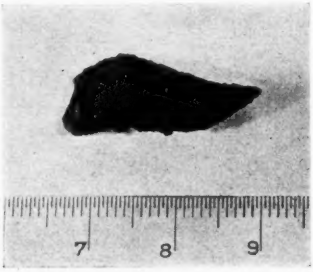

Fig. 146.—Bone removed from lower left bronchus, external branch, after a sojourn of three and one half years.

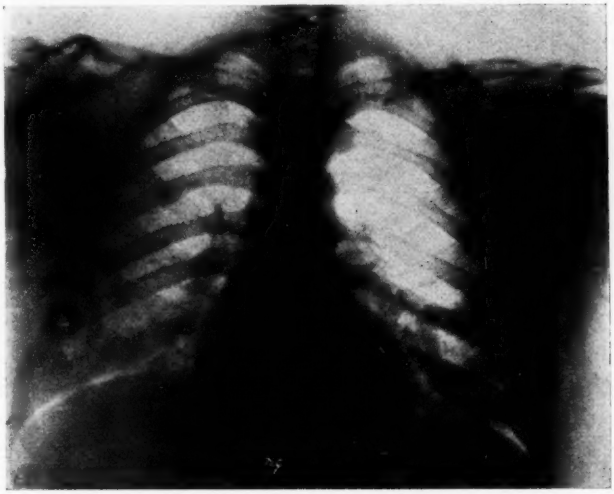

Fig. 147.—Case III. Showing evidence of extensive lung suppuration—left lower lobe. The foreign body cannot be made out.

completely obstructing the lumen of the bronchus, were to be seen. The pus, and later the blood from the granulation tissue, obstructed the view so that it was necessary to bronchoscope the

patient three times before the foreign body, a piece of beef bone, could be safely removed (Fig. 146).

Although the foreign body had been removed, the extensive suppuration continued. The patient was daily expectorating a large quantity of almost pure pus. There was a large bronchiectatic cavity with several ramifications from which this large amount of exudate was coming. Bronchoscopic irrigation would benefit the patient for only one day. He was later seen by Dr. H. Neuhof, who operated upon him. The operation com-

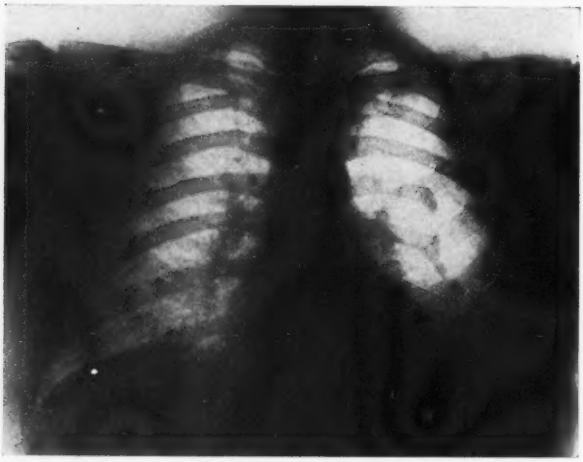

Fig. 148.—Case III. Same patient ten months after surgical cure of extensive lung suppuration.

pletely cured the suppurative process, and converted an unhappy invalid into a healthy and able-bodied man (Figs. 147, 148).

Case IV.—A man, age forty-seven, had been suffering with severe coughing spells and the expectoration of large quantities of purulent sputum for the past three years. He had lost 30 pounds in the last seven months, and recently suffered a pulmonary hemorrhage. He had been treated for asthma and tuberculosis before he was referred by Dr. Walzer for bronchoscopy. Bronchoscopy demonstrated a marked dilatation of all the visible

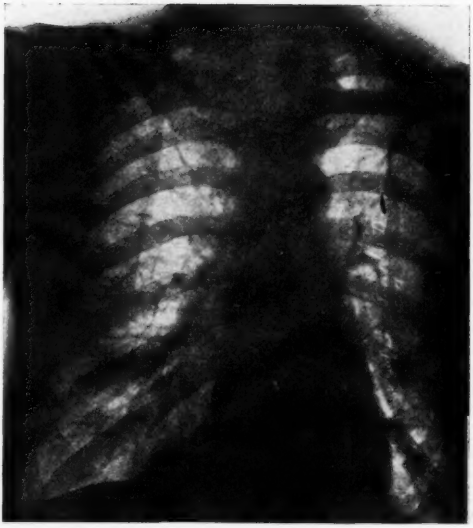

Fig. 149.—Case IV. Postero-anterior film of patient with extensive lung suppuration left lower lobe, behind heart.

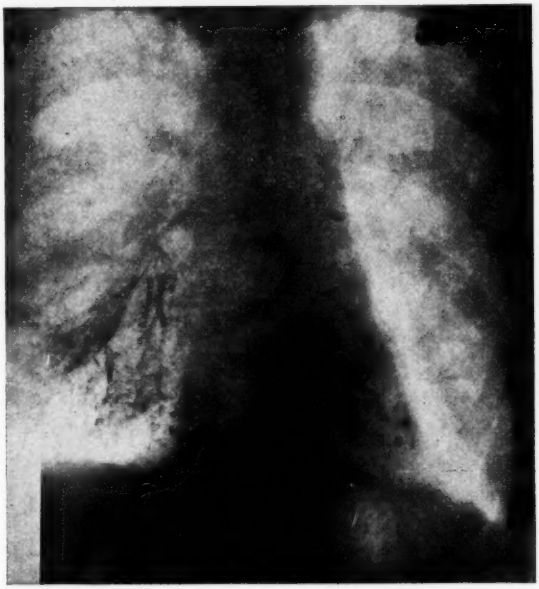

Fig. 150.—Case IV. Same patient as Fig. 149 after introduction of lipiodol into diseased area. Many bronchial dilatations are to be noted.

bronchial elements of the left lower lobe. The Roentgen film, however, did not demonstrate this lesion. By the introduction of lipiodol into this area, we were able to demonstrate a number of bronchiectatic cavities situated behind the heart (Figs. 149, 150). It is for the demonstration of a lesion in this region that lipiodol is of particular value. Bronchoscopy affords this patient comfort for only two days. Some more promising form of treatment must be considered if we are to relieve this patient of his suffering.

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EMBOLISM AND THROMBOSIS OF THE ABDOMINAL AORTA. REPORT OF FIVE CASES

EMBOLISM and thrombosis of the abdominal aorta has occurred most frequently during the course of chronic cardiac and arterial disease, the great majority of these being in association with mitral stenosis and auricular fibrillation. That such embolism and thrombosis, according to Wylde,[49] from this source (mitral stenosis with auricular fibrillation) is not more frequent is probably due to the narrowing of the mitral orifice, thus preventing a clot of larger size passing through.

The source of emboli in cases of uncomplicated cardiac disease is usually cardiac thrombi. Cardiac thrombi are of two types: The small and mycotic (vegetations) are usually associated with an active endocarditis, and, as a rule, occur on the valves, but they may also be mural; the second, a larger type of thrombi, is usually found where the circulation is the slowest, as in the auricular appendages and apices of the ventricles between the columnæ carni. This last type is especially prone to occur when there is a chronic failure of compensation. A peculiar and rare form of cardiac thrombus is that known as the ball thrombus and, when present, was found (in Welch's[47] series) always in the left auricle and in association with mitral stenosis, except in one instance in a case of aortic stenosis with insufficiency of the mitral, reported by Stenge.[41]

The portion of the abdominal aorta usually affected by an embolus and thrombus is that below the origin of the mesenterics. The plug usually occupies the lower end of the aorta, and extends

a variable distance into the arteries below. Secondary thrombi are not uncommon in the arteries given off from the occluded portion of the aorta, and such thrombi are frequently found to extend into both iliacs and variable distances into the arteries of the extremities. In some instances the plug has been known to involve the entire abdominal aorta, and extend into the renal, the mesenterics, and celiac axis, as in the case reported by Saltykow,[36] and he was able to find 17 other such cases.

In the 59 cases collected by Welch up to 1899, the thrombus extended into the common iliacs in all of the instances, and in many into the arteries lower down, sometimes even as far as the posterior tibial, the end being lower usually on one side than the other. Welch divided his 59 cases into 45 referable to embolism, and 14 due to thrombosis. The source of the embolus was believed to have been in the heart in 35 cases; aneurysm of the ascending aorta in 1; pressure of a tumor on the aorta in 2; atheroma of the thoracic aorta in 1; it was undetermined in 6. The heart was found normal in 11; mitral stenosis was present in 20 cases; acute mitral endocarditis in 3; mitral endocarditis not further defined in 4; mitral insufficiency without stenosis in 1; thrombus in the left auricle without valvular disease in 1. Thrombi in the left ventricle, mostly without valvular disease, in 8; and large aortic vegetations in 1. Thus it will be seen that fully one-third of the cases were associated with mitral stenosis. In a few of the cases a congenital narrowing of the abdominal aorta was noted (Welch[47] and Oestreich[32]). In 3 instances, plugging of the abdominal aorta was associated with embolism or thrombosis of the upper extremity. This was present in 3 of our cases. Hemorrhagic infarction of the intestines was noted in 1 case of Welch's series. Similar cases were reported by Oestreich,[32] Keilty,[18] and Saltykow.[36] It was also present in one of our cases. In some cases hemorrhages of the mucous membrane of the bladder and uterus were found at necropsy. A case of occlusion of the abdominal aorta followed by hemorrhagic infarction of the uterus was reported by Danisch.[6]

A number of cases have been reported since Welch's summary of the literature in 1899 (see Bibliography). Hesse[15] in 1921

collected 73 cases. These included 41 cases mentioned by Welch, and to these he added 32 others. The majority of the cases were due to endocarditis, principally mitral stenosis.

But Wylde in 1922 reported 2 cases, and states that he was able to collect 94 cases from the literature including his. Since 1922 we have found the following cases reported in the literature: Aubertin,[2] 2 cases; Huisman,[17] 1 case; Lundblad,[26] 2 cases; Turreti and Guder,[44] 1 case; Somalo,[39] 1 case; Danisch,[6] 1 case; Menasci,[28] 1 case; and Tscherwakoff,[43] 1 case of his own, and he quotes Spassokukotzky[40] as reporting a case of thrombosis of abdominal aorta following iodoform poisoning. These, added to the 94 Wylde was able to collect, makes a total of 105; while we think that this is a fairly complete list, it is possible that a few more have been reported.

The majority of the cases were in association with chronic heart and arterial diseases, over 50 per cent. of these being definitely mitral stenosis with auricular fibrillation. Plugging of the abdominal aorta in more rare instances has occurred after acute infection, as rheumatic fever, puerperal infection, erysipelas, typhoid fever (Forguese); pneumonia (Leyden[22]); influenza (Menasci[28]); umbilical infection in childhood (Moschowitz[30] and Wheler[48]); aneurysm of the aorta, arteriosclerosis, and syphilis.

To these we wish to add 5 cases. All of the cases occurred in females, the youngest being seventeen; the 4 others varying between forty and fifty-eight. All were fibrillating and had signs of cardiac failure. Four of the cases of auricular fibrillation were associated with a mitral stenosis, and 1 with a hypertensive cardiovascular disease. All were fatal. The duration varying from a few days to forty-four days. Before developing the Rider's embolus and thrombus, 3 of the cases showed the clinical picture of embolism to other vessels, namely: The vessels of the upper extremity in 3 cases; a cerebral, pulmonary, and splenic embolus in 1 case each. In 1 of the cases necropsied a mesenteric embolism was found.

Case I.—This patient (E. G.), a housewife, age fifty-one, was admitted to the Long Island College Hospital on October

20th, complaining of severe pains in the legs from the knees down, coldness of both legs, marked precordial distress, and palpitation of the heart.

The patient had two attacks of diphtheria, one at the age of two, and the other at ten. The second attack was severe, and confined her to bed for one month. Three months later she developed chorea which lasted for three months. She was well then until the age of forty-one, when she developed palpitation, precordial pain, and shortness of breath. Under treatment and rest in bed these symptoms disappeared, and she was free from complaints until fifteen months before admission. She passed her menopause two years ago with no difficulty.

Present illness: Fifteen months prior to admission, she complained of severe pain in the knees, calves, and arms, and tired easily on walking a few blocks. She also had some pain in the precordial region. She was told by a doctor that she had heart trouble, and was under his observation for one year. When she was sitting in a chair and on attempting to get up, felt a sudden, sharp, knife-like pain in her left leg, from the knee down; pain lasted one half hour and disappeared. She was admitted to a hospital and remained four weeks. She had no recurrence of her pain, but her leg remained cold, and when she walked a few blocks she had to stop on account of pain in the calves of her legs. She was under observation for two months with the same complaint. Three days before admission to Long Island College Hospital, the pain in her left leg increased and she lost all sensation below her knee. It felt like a "piece of wood," except that she had knife-like pains in her calf.

Her leg felt cold and the sole of the foot felt like a sponge. On the day of admission she felt severe knife-like pains in both legs, from the knees down; both legs and feet felt ice-cold, and she had no sensation. Symptoms of palpitation and precordial distress were complained of.

On admission, the patient had a temperature of 97° F. (rectal), pulse 76, and respirations of 30. It was noted that the sclera was clear. There was a moderate gum-edge infection. The lungs were clear, not even showing basal râles. The

apex-beat of the heart was diffuse, best felt in the fifth intercostal space. The left border percussed 15 cm. from the midsternal line in the fifth intercostal space. There was a definite presystolic thrill palpable at the apex. The apical rate was counted as 98 and irregular (the pulse rate being 76). There was a loud systolic murmur at the apex poorly transmitted. The pulmonic second sound was accentuated and louder than the aortic second sound. Abdominal examination revealed no tender points, rigidity, or evidences of fluid. The hepatic and splenic edges were not felt. Both lower extremities were cold and blue from the knees down, and there was complete loss of sensation on both sides from a point 2 inches above both knees. The patient had no power in either leg and was unable to lift them off of the bed. The knee-jerks, however, were very active. Pulsations were not obtained in either femoral, popliteals, or in the vessels of the feet.

Laboratory Data.—Red blood-cells, 4,000,000; white blood-cells, 16,000; polymorphonuclears, 76 per cent.; lymphocytes, 24 per cent.; hemoglobin, 76 per cent. (Sahli); Wassermann negative; blood-pressure, 110/65.

Urine: Albumin was present to the extent of 0.2 per cent. to 0.5 per cent., and granular casts were noted on several occasions, although the specific gravity varied between 1.014 and 1.025. The blood-chemistry revealed a urea nitrogen 37.50 mg. per 100 c.c.; urea, 80.3 mg.; uric acid, 4.53 mg.; sugar, 133.00 mg., and creatinin, 1.50 mg.

The electrocardiograph tracing confirmed the diagnosis of auricular fibrillation.

The opinion arrived at clinically was that of a mitral stenosis with myocardial insufficiency, and auricular fibrillation complicated by a Rider's embolus and thrombus at the bifurcation of the abdominal aorta. During her stay in the hospital, the blueness increased, both feet becoming black and gangrenous (Fig. 151), both legs a deep purple in color, and the right thigh blue and cyanotic. This change was not accompanied by any rise in temperature, except a terminal rise to 101° F. (rectal) just before death. During this time she complained of severe

paroxysmal attacks of pain in both legs. This was not relieved by morphin. She became gradually weaker, abdomen became more distended, pulse was very weak and irregular. She was

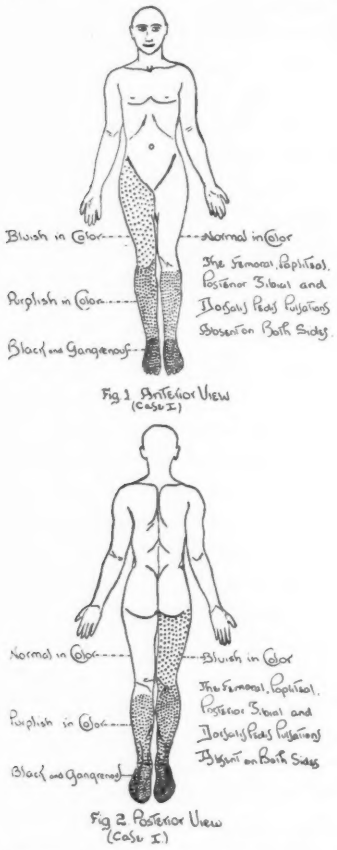
Bluish in Color
Normal in Color
The Femoral, Popliteal, Posterior Tibial and Dorsalis Pedis Pulsations Absent on Both Sides.
Purplish in Color
Black and Gangrenous
Fig 1. Anterior View (Case I.)
Normal in Color
Bluish in Color
The Femoral, Popliteal, Posterior Tibial and Dorsalis Pedis Pulsations Absent on Both Sides
Purplish in Color
Black and Gangrenous
Fig 2 Posterior View (Case I.)

Fig. 151.—Extent of gangrene and discoloration in lower extremities on day of death.

covered with a cold, clammy perspiration. Incontinence of urine developed, she became semiconscious, and finally died thirteen days after admission.

Autopsy Report by Dr. Archibald Murray.—The autopsy was performed two hours after death. Body is poorly nourished, rigor mortis not yet developed. The right foot is black in color, dry and gangrenous in appearance (Fig. 151). The right leg is dark purple up to about 2 inches below the patella; the rest of the leg and the thigh are bluish in color. The left foot is black in color and similar to the right. The left leg is dark purple up to about 4 inches below the patella. The rest of the leg and the thigh are normal in color and appearance. There is no pitting on pressure, but a dry hardness to the skin and underlying tissues. Nothing of note was found in the mediastinum, and there was no evidence of infarction in the lungs. Heart is moderately enlarged, and the epicardial fat increased in amount. Left ventricle is smaller than normal, and the walls are thickened. The mitral valve is thickened and shows stenosis—admits only one finger.

The left auricle contains a large thrombus. The right heart is dilated, and walls are thin. The aorta shows numerous areas of atheroma. Only one coronary artery could be found. No infarcts were present. Spleen is small, weighs 70 gm. Left kidney weighs 160 gm., is congested, and contains numerous infarcts varying in age and size. Right kidney weighs 90 gm. and resembles the left. Stomach appears normal. Duodenum shows a small ulcer about 3 mm. in diameter, with raised edges and a necrotic base, situated about 4 cm. below the pylorus. The liver weighs 1050 gm. and appears normal. Gall-bladder normal. Pancreas and intestines apparently normal. A mural thrombus is present at the lower end of the abdominal aorta, extending by two prolongations into both common iliacs, there being more thrombus present on the right side than on the left. Thrombosis begins about the middle portion of the femorals, and extends downward through the popliteals on both sides as far as the upper third of the legs. Both arteries below the middle third of the legs were soft, patent, and not thrombosed. The arteries of the lower extremities show no evidence of disease.

Microscopic.—Thrombus of left auricle: The greater part of

the thrombus is white. Along the lines of Zahn are collected many polymorphonuclears in some portions of the thrombus. One area of this sort, on the free surface, suggests an infectious process, but, in general, the leukocytes are not present in large numbers, and the thrombus appears to be bland.

Spleen: The follicles are intact; the arterioles show hyaline thickening of the walls. The venules are distended with blood, and small hemorrhages are seen. The pulp contains numerous polymorphonuclear cells.

Kidney: There are many indistinctly outlined hemorrhagic infarcts scattered throughout the cortex. There is an infiltration of polymorphonuclear cells in some places at the margins and within the infarcts; in other areas no cellular reaction is seen. The capillaries in the tissue surrounding the infarcts and throughout the medulla are congested. Some of the tubules outside of the infarcts show swelling and necrosis; others are filled with polymorphonuclear cells. No bacterial masses are seen in the glomeruli or vessels.

Case II.—The patient (E. O.), was a housewife, age forty-two, and admitted to the Long Island College Hospital on November 2, 1926, complaining of shortness of breath, smothering spells, palpitation, excruciating pain in both calves of her legs, cough, and a blood-tinged sputum. As a child she suffered with chorea.. There was no history of rheumatism or sore throat. For the past ten years she had some shortness of breath on exertion, but got along fairly well by avoiding overwork or strenuous exercise. She was a well developed female, markedly cyanotic and orthopneic on admission. A marked degree of gum-edge infection was present. There was dulness at the right base with numerous moist râles at either base. There was a well localized heart apex impulse, best felt in the fifth interspace 12 cm. from the midsternal line, but could be felt in the sixth interspace also. There was quite a forceful thrust, although a systolic shock was present. There was an irregularity present in the nature of a fibrillation. The left border percussed 13 cm. from the midsternal line, the right 4 cm. and the arch

7 cm. in the second intercostal space. The first sound was loud and abrupt, followed by a systolic first, not loud and not well transmitted. There was a double-phase diastolic murmur that sometimes ran into the first sound and occasionally not. There was a little reduplication of the second sound. The pulmonic second sound was greatly accentuated and was louder than the aortic second. The hepatic edge was just palpable, and was tender. The lower extremities were warm, and had good color. There were no pulsations palpable in the dorsalis pedis or posterior tibial in the left foot. There was considerable tenderness in the calf muscles, more marked on the left.

Laboratory Data.—Red blood-cells, 3,650,000; 68 per cent. hemoglobin (Sahli); white blood-cells, 14,000; polymorphonuclears, 85 per cent.; lymphocytes, 15 per cent.; Wassermann negative; urine, faint trace of albumin. Blood-pressure varied from 130 to 150 systolic, and 85 to 90 diastolic. The pain in her legs and all other symptoms gradually subsided, her irregularity persisted, although her rate decreased from 112 on admission to 80. Fifteen days after admission, on November 17th, she complained of severe pain in the left abdominal region, causing her to cry out with pain, and coincident with this her color became pale, lips very cyanotic, and her body was covered with a profuse perspiration. Following this, she fell into unconsciousness, her breathing became stertorous, she had incontinence of the bowel and bladder. Examination at this time showed a smoothness of the right face, the left corner of the mouth was drawn upward, and the right arm and leg were limp, and there was a positive Babinski on the right. Within two hours she could be aroused, but was unable to speak. Within forty-eight hours she practically recovered, except for some weakness of the entire right side. An opinion was passed at that time of a cerebral embolism. She continued to improve, and her radial rate decreased to 68. Her rhythm remained irregular, and she was discharged on January 11, 1927.

While at home the patient remained well compensated, and was practically free from complaints, when on February 8th, as she was getting out of bed, she was suddenly seized with severe,

excruciating pain in the calves of either leg and the lower extremities became cold and numb. She also had pain in her right hand. She was rushed immediately to the hospital.

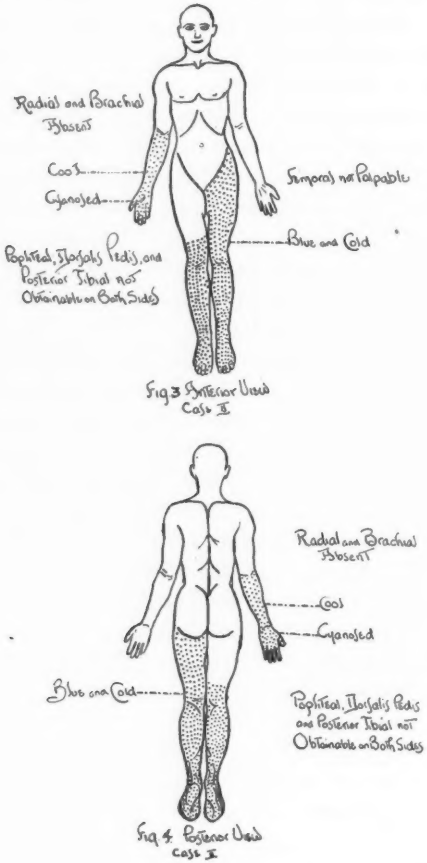
Radial and Brachial Absent
Cool
Cyanosed
Femoral not Palpable
Blue and Cold
Popliteal, Dorsalis Pedis, and Posterior Tibial not Obtainable on Both Sides
Fig 3 Posterior View Case II
Radial and Brachial Absent
Cool
Cyanosed
Blue and Cold
Popliteal, Dorsalis Pedis and Posterior Tibial not Obtainable on Both Sides
Fig 4 Posterior View Case II

Fig. 152.

On examination the patient was found to be pale and cold. The heart apex was in the fifth interspace, rhythm very irregular, the rate at the apex being 160, and 88 at the wrist. There was

a to-and-fro murmur at the apex, not well transmitted. The abdomen was distended, and there was considerable tenderness in the right side in line with the umbilicus. The hepatic edge was felt four fingers below the costal margin, and was very tender.

The right arm felt cool, and the hand was slightly cyanosed. The right radial and brachial pulsations were absent (Fig. 152). The entire left lower extremity was blue and cold up to the inguinal region. The right was cool up to 4 inches above the knee. The left femoral pulsation was not present; the right, however, was palpable. The pulsations in both popliteals, dorsalis pedis, and posterior tibial vessels were not obtained. There was complete loss of sensation on the left side to cotton

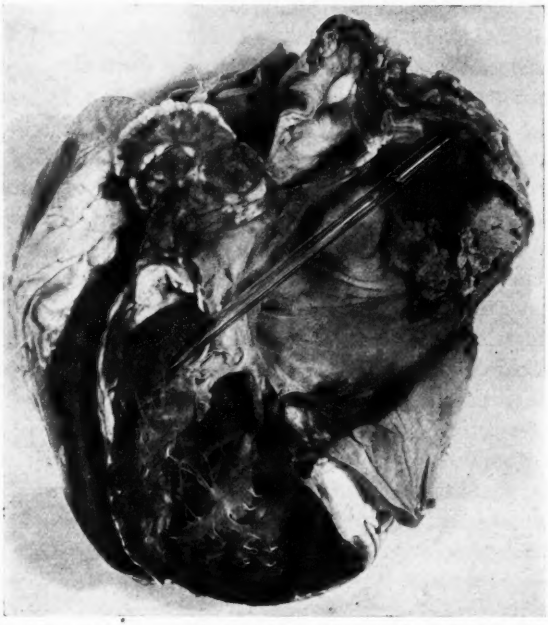

Fig. 153.—A large mural thrombus and several small thrombi in the left auricle. Mitral orifice is thickened and distorted, admitting only one finger. (Case II.)

and a sharp point, from 3 inches below Pouparts ligament on the left side.

The white blood-count at that time was 26,800, with 86 per cent. polymorphonuclear cells. The patient's temperature gradually rose to 103° F. (rectal), she became stuporous and cried out frequently with pain, both in her legs and abdomen. Vomiting occurred, which soon became fecal in character. She weakened rapidly, became unconscious, and died February 10th. It was thought that the patient had a mitral stenosis with myocardial insufficiency complicated by an auricular fibrillation, a rider's embolus at the bifurcation of the abdominal aorta, etc., an embolus to the right arm, and a mesenteric embolus.

Autopsy.—The body is that of a poorly nourished, middle-aged female. There is marked cyanosis of both lower extremities, and the abdomen is much distended (Fig. 152). The heart contains a large mural thrombus (Fig. 153) and several smaller thrombi in the left auricle. The mitral orifice was thickened and distorted, admitting only one finger. The myocardium is soft and pale and the chambers are dilated. There was a conical-shaped thrombus in the abdominal aorta extending 8 cm. from the bifurcation, and filled the left common iliac and first parts of the femoral and hypogastric arteries. The right hypogastric is also thrombosed. A large area of the jejunum is gangrenous as the result of a mesenteric thrombosis. The liver shows a passive congestion. The spleen contains several recent infarcts. There are also several small infarcts in the left kidney. The lungs show congestion, edema, and much anthracosis.

Case III.—Mrs. M. Q. was a housewife, age fifty-eight, admitted to Long Island College Hospital March 2d, complaining of "palpitation; marked shortness of breath, and pain in the left foot." Three years before admission, the patient had what was called "LaGrippe," and two weeks following this she contracted pneumonia. From that time on she began to experience difficulty in walking upstairs, and was conscious of palpitation with occasional choking sensations. She was told by her doctor she had "heart trouble." One year before entrance she noticed

for the first time that she had edema of her ankles, that it was more marked at night, and disappeared with rest. About this time her dyspnea increased to the extent that her sleep was disturbed. One month prior to entrance she fell and injured her ankle. Her symptoms gradually increased till admission to the hospital.

On admission the patient was dyspneic and slightly cyanosed, the neck veins were full, but there were no abnormal pulsations noted. The chest was emphysematous in type, and moist râles were heard at both bases. The apex-beat was seen and palpated at fifth intercostal space, 11 cm. from midsternal line. No shocks or thrills were palpated. The left border was percussed $11\frac{1}{2}$ cm. from the midsternal line, and the right 3 cm. from the midsternal line. First sound was clear at the apex, the second sounds were about equal. There was a slight systolic murmur at the apex, not well transmitted. There were no murmurs at the base. The rhythm was irregular. The rate at the apex was counted as 140, while that at the radial was counted as 100. The abdomen was distended, and marked tympanites was present. No fluid wave or flank dulness was obtained. The hepatic edge was palpated three fingerbreadths below the costal margin, and was very tender. The spleen was not palpated. Examination of the extremities showed slight ankle edema, normal deep reflexes, and considerable radial wall change.

Laboratory examination showed a negative blood Wassermann; red blood-cells, 4,800,000; white blood-cells, 6800; polymorphonuclears, 72 per cent.; lymphocytes, 28 per cent.; hemoglobin, 83 per cent. (Sahli); blood-chemistry, normal; blood-pressure varied between 190 and 240 systolic, and diastolic between 100 and 120. The urine showed no albumin, no casts, with the specific gravity varying between 1.012 and 1.020; phthalein output, 45 per cent. in two hours.

The clinical opinion was that of arteriosclerosis with hypertension, myocardial insufficiency, and auricular fibrillation. With rest, digitalis, and diet she improved. Her palpitation and dyspnea were negligible while in bed. Her apex rate was 76, but still irregular, and her pulse rate was 60. She continued to

improve and was discharged on March 24, able to be up and about with no discomfort.

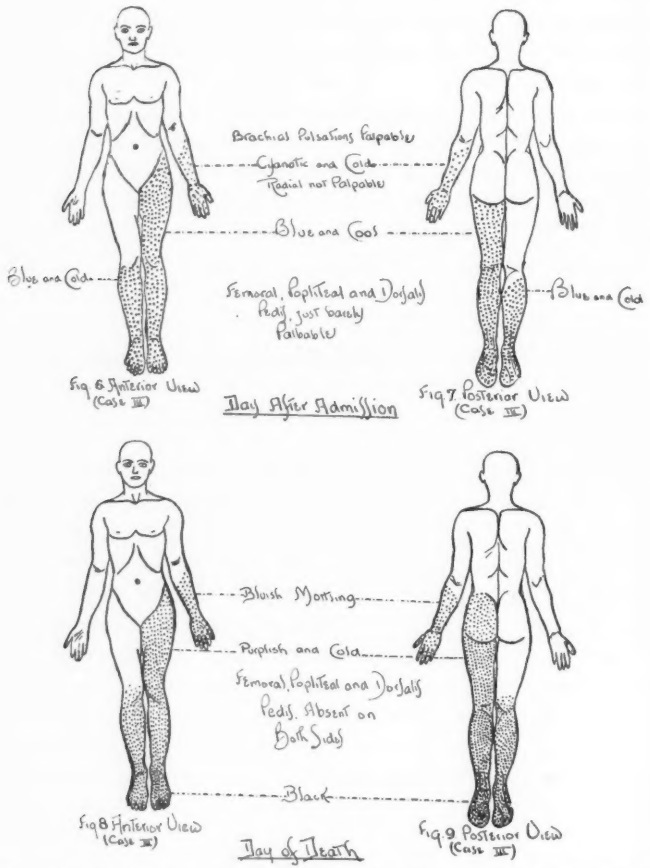
Brachial Pulsations Palpable
Cyanotic and Cold
Radial not Palpable
Blue and Cool
Blue and Cold
Femoral, Popliteal and Dorsalis Pedis just barely Palpable
Blue and Cold
Fig 6 Anterior View (Case III)
Day After Admission
Fig 7 Posterior View (Case III)
Bluish Mottling
Purplish and Cold
Femoral, Popliteal and Dorsalis Pedis Absent on Both Sides
Black
Fig 8 Anterior View (Case III)
Day of Death
Fig 9 Posterior View (Case III)

Fig. 154.—Showing extent of gangrene and changes in vessel pulsation in Case III on admission and day of death.

The patient remained well compensated for nine months, being able to do her own housework, when, three weeks before her second admission, January 9th, she was seized with excruciat-

ing pain in both lower extremities from the thighs down, more pronounced in the right. Numbness in these extremities as well as a feeling of coldness existed. She also had some pain, coldness, and numbness in the left arm. These symptoms persisted until admission. On admission, the patient had a temperature of 103° F., a pulse of 160, and respiration of 45. She was slightly cyanosed—especially in the fingertips—cold, clammy, and bathed in a diffuse perspiration. There were numerous moist râles in either base. The apex impulse was very forcible in the fifth intercostal space, 11 cm. from the midsternal line and markedly irregular; no shocks or thrills were palpated. The left border was percussed 11½ cm. from the midsternal line, and the right

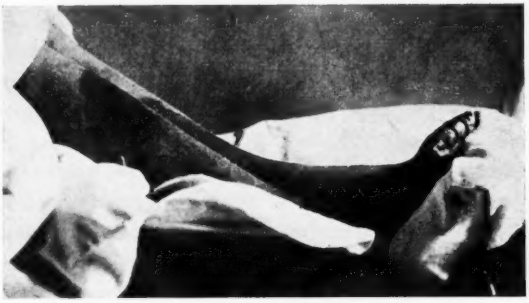

Fig. 155.—Extent of gangrene ten days after onset. Case IV.

4 cm. The second sounds were about equal. A systolic blow was heard at the apex, poorly transmitted, and no murmurs were heard at the base. The abdomen was distended and tympanitic. There were no areas of tenderness, except the slightly tender liver which extended 2½ fingerbreadths below the costal margin.

The spleen was not palpated. The right lower extremity was a purplish blue, and cold from the knee down (Fig. 154), the left lower extremity was cold from knee down, and cool from the hip to the knee. It took on a purplish blue from the hip to the knee, and was blue from knee down. In the left leg there was marked loss of sensation, the deep reflexes were not obtain-

able, and she was unable to use the limb. On admission the vessel pulsations in the lower extremities were just palpable, but two days later the blueness and coldness had increased, and all pulsations from the femorals down were absent. The left arm did not have the same power as the right, it was colder and the reflexes were diminished. The radial pulsation was not obtained, but a pulsating brachial vessel could be felt. Both the forearm and hand were slightly cyanosed (Fig. 154). Blood examination showed: Red blood-cells, 2,770,000; white blood-cells, 15,400; polymorphonuclears, 91 per cent.; hemoglobin, 60 per cent. (Sahli); Wassermann, negative; blood-pressure varied from 140 to 190 systolic, and from 90 to 130 diastolic. The patient's general condition grew gradually worse, the color deepened in either lower extremity as shown by Fig. 154, and the color of either foot was almost black. Her temperature gradually rose to 105° F., and she died two days after admission, with no necropsy permit being obtained. The clinical opinion was expressed of arteriosclerosis with hypertension, myocardial insufficiency, auricular fibrillation complicated by a Rider's embolus and thrombus at the bifurcation of the abdominal aorta, and an embolus involving the left upper extremity. Although no necropsy was obtained in this case, we felt that the above diagnosis was justifiable in view of the similarity to the clinical picture of Cases I and II; namely, history of cardiac disease with auricular fibrillation, sudden onset, with obliteration of vessel pulsation in both lower extremities, with subsequent development of gangrene and embolic phenomena in the left arm.

Case IV.—Mrs. M. T., a housewife, age forty, was admitted to Long Island College Hospital July 1st, complaining of pains over the heart region, attacks of suffocation, and pains in all extremities. As a child she had measles, whooping-cough, and frequent attacks of tonsillitis. At the age of twenty-four she had an attack of acute rheumatic fever, recovering with no complications. Six years later she had a recurrence of the rheumatic fever, and at this time she was told that she had a weak heart.

She subsequently went through two pregnancies with no grave complications. Three years prior to her admission she commenced to suffer with some precordial pain, dyspnea on the slightest exertion, and attacks of dizziness with spots before her eyes, but was able to carry on her household duties. Two weeks before her admission, her dyspnea became marked, she developed a cough accompanied by hemoptysis; at this time she experienced, upon deep inspiration, a severe pain all over her chest. One week before admission she suddenly experienced severe pain in both tibial regions and in both hands, to the extent that sleep was disturbed.

On admission she was found to be a well developed and nourished female of forty, with a normal temperature, pulse 88, and respirations 33. She was orthopneic and had to be propped up in bed. There was a maculopapular eruption over her forehead, face, and body. There were two small, crusted ulcers (0.5 cm. in diameter) just to the left of the xiphoid. Her teeth were poor and carious; tonsils large, cryptic, and infected. An anterior, bilateral, cervical adenopathy was present, shotty in type. The thorax was symmetrical, tactile fremitus was diminished over both bases, resonance was impaired, breath sounds were diminished, and many moist râles heard there. The apex was seen and felt in the fifth intercostal space, 12 cm. from the midsternal line. The rhythm was regular. There were no shocks or thrills. The left border percussed out $12\frac{1}{2}$ cm. from the midsternal line, and the right $3\frac{1}{2}$ cm.

The first sound was quite snappy, the pulmonic second sound was a little louder than the aortic second. There was a definite presystolic murmur at the apex, and a systolic murmur transmitted into the axilla. No murmurs were heard at the base. There was some tenderness in the right upper quadrant, although the liver was not palpated. The splenic edge was palpated just below the costal margin and was tender; no fluid wave was present, nor was there any dulness in the flanks. The lower extremities had a good color; there was no pretibial edema, but there was considerable tibial tenderness on pressure. Deep reflexes were present and equal.

Laboratory Data.—Red blood-cells, 3,975,000; white blood-cells, 6700; polymorphonuclears, 73 per cent.; lymphocytes, 21 per cent.; degenerates, 2 per cent.; eosinophiles, 2 per cent.; transitionals, 2 per cent.; hemoglobin, 75 per cent. (Sahli). Blood chemistry normal; Wassermann, 4 plus; urine examination was negative, with a specific gravity varying from 1.017 to 1.026; phthalein output was 42 per cent. in two hours; blood-pressure, 112/78.

After seven days' stay in the hospital all of her symptoms subsided, and she insisted upon going home. She was discharged with instructions that her luetic infection be treated and her infected tonsils and teeth be cared for.

The clinical opinion expressed at that time was a chronic rheumatic endocarditis with mitral stenosis and regurgitation, myocardial insufficiency, and secondary lues.

For fourteen months the patient was fairly comfortable, being able to do light housework, when, two weeks before admission, she was suddenly seized with marked shortness of breath, marked precordial pain, and bloody sputum. She also complained of diminution of urinary output for a period of several days. These symptoms persisted, and when she was admitted to the hospital she was found to be cyanotic, orthopneic, respirations very labored, and was expectorating a frothy, blood-tinged sputum. Her tonsils and teeth were still in the same poor condition.

A flat note was percussed at both bases, breath sounds were absent, and moist râles were heard below either scapula. The apex-beat was seen in the fifth intercostal space in the anterior axillary line, 12 cm. from the midsternal line, the rhythm being irregular. The left border percussed $12\frac{1}{2}$ cm. from the midsternal line, the right border $4\frac{1}{2}$ cm. On auscultation the rhythm was irregular, the rate being 120 (radial rate, 100). The pulmonic second sound was accentuated and louder than the aortic second. A systolic murmur was audible at the apex, and transmitted to the axilla. The hepatic edge was palpated three fingerbreadths below the costal margin, and was very tender, likewise the spleen was palpated two fingerbreadths below the

costal edge, and was very tender. There was a generalized shotty glandular adenopathy.

Laboratory findings at this time were: Red blood-cells, 4,150,000; white blood-cells, 33,000; polymorphonuclears, 88 per cent.; eosinophiles, 1 per cent.; lymphocytes, 11 per cent. Blood pressure, 105/70; blood culture, sterile; Wassermann, 4 plus; urine, trace of albumin; specific gravity varied between 1.018 and 1.026; phthalein output, 55 per cent. in two hours.

The patient was put under digitalis therapy, and within two days her apex rate decreased to 88 and radial rate to 80. At this time she complained of pain in the right lower chest, exaggerated by deep inspiration and cough. Examination revealed a to-and-fro friction rub in the posterior axillary line. This was interpreted at the time as being due to a pulmonary infarct, and clinically behaved as such. Eight days later a sudden pain was experienced in the left "kidney region." The following day she complained of severe pain and numbness in the right hand, and pain in the right foot. The right radial and ulnar pulsations were not obtained at this time, having been present previously. The right hand was much cooler than the left, and the right foot was cooler than the left. The right dorsalis pedis pulsation was felt with difficulty, while the pulsations were present in the posterior tibial and in the vessels of the left foot.

The right knee-jerk was diminished, while the left was very active. The very next day, she experienced sudden severe pain in the left groin, radiating downward to the tips of her toes, and had a sensation of numbness and coldness in that extremity. This entire limb felt cold, and was blue from the knee down. The left femoral, popliteal, dorsalis pedis, and posterior tibial pulsations were not obtained. The right femoral pulsation was present, but the popliteal, dorsalis pedis, and posterior tibial pulsations were absent. The right knee-jerk was present, but the left was absent. There was a beginning gangrene in the left leg, with scattered blue, blotchy areas in the right leg. Six days later, gangrene was present in the lower two-thirds of either leg (Fig. 155) and extended gradually up to the middle of both thighs (Fig. 156). All during this time the patient suf-

fered with excruciating pain in both lower extremities. She became involuntary, grew gradually weaker with the extension

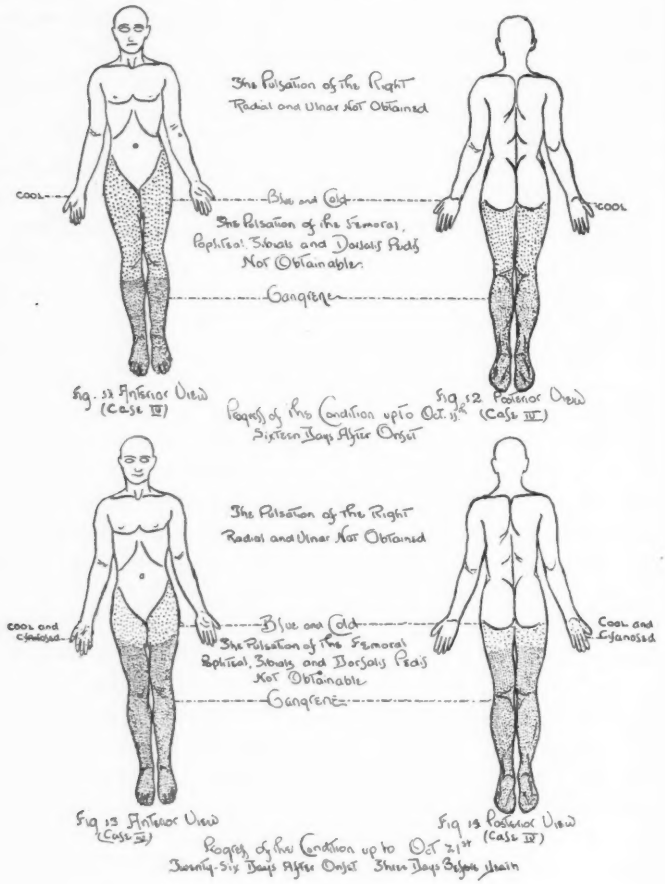

Fig. 156.

of the gangrene, and died as the gangrene reached beyond the mid-thigh region (Fig. 156), twenty-nine days after onset.

An opinion was expressed clinically as that of a tertiary lues;

chronic rheumatic endocarditis with mitral stenosis; auricular fibrillation, and myocardial insufficiency complicated by multiple embolism (pulmonary, splenic, left upper extremity, and Rider's embolus and thrombosis of the abdominal aorta).

Case V.—The patient, L. M., an unmarried girl of seventeen, was admitted to Long Island College Hospital on April 27, 1927, complaining of: Shortness of breath, palpitation, pains in both legs and feet, numbness of both feet, and coldness of the right foot and leg.

At the age of nine she had an attack of acute rheumatic fever that lasted for two months. She made an excellent recovery, but nine months later she developed dyspnea, palpitation, and precordial pain. She was in bed again for two months and was told at that time that she had "heart trouble." She resumed her usual school duties, with certain restrictions, and was comparatively comfortable until seven weeks before admission, when she was suddenly seized with an attack of marked weakness after which she collapsed. She was taken home in a taxi, and climbed two flights of stairs. She became very cyanotic after this exertion and again collapsed. When revived, she vomited and complained of marked fulness in the abdomen. She remained in bed for two weeks. Then, when she got out of bed, the thing first noticed was numbness in her left foot. It was emphasized that there was no pain at that time. This lasted for three days. On April 12th, fifteen days before admission, she developed a severe, sharp stabbing pain in the calf of the right leg, which lasted for three hours. Morphin was required to control her pain. The leg has been numb and cold since then, and there have been recurring pangs of severe pain in this leg. Two days later the toes became blue; within a few days the toes became gangrenous, and the leg and thigh blue and cold.

On admission, her temperature was 98.6° F., pulse 108 (irregular), and respirations were 24. There was marked cyanosis, and the sclera was icteric. The tonsils were diseased. The chest percussed resonant, but there were numerous moist râles

at either base. There was a diffuse irregular impulse over the precordium, the apex impulse was seen best in the fifth inter-

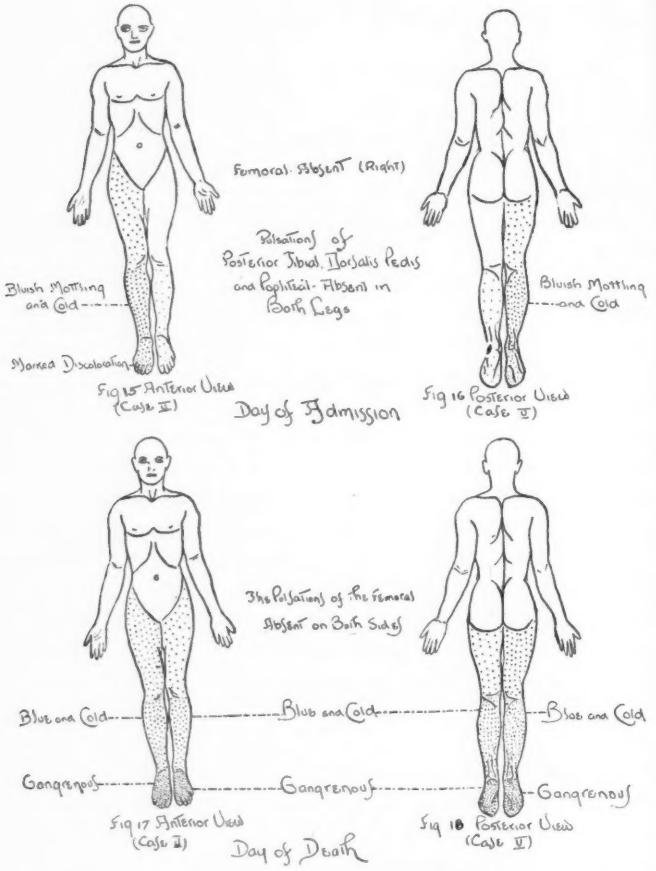
Femoral Absent (Right)
Pulsations of Posterior Tibial, Dorsalis Pedis and Popliteal Absent in Both Legs
Bluish Mottling and Cold
Marked Discoloration
Fig 15 Anterior View (Case II)
Bluish Mottling and Cold
Fig 16 Posterior View (Case II)
Day of Admission
The Pulsations of the Femoral Absent on Both Sides
Blue and Cold
Blue and Cold
Blue and Cold
Gangrenous
Gangrenous
Gangrenous
Fig 17 Anterior View (Case II)
Fig 18 Posterior View (Case II)
Day of Death

Fig. 157.—Showing progress of gangrene during the fourteen days between admission and death.

costal space. The left border percussed in the anterior axillary line, and the right 5 cm. from the midsternal line.

There was a double murmur at the apex, and a short systolic blow was heard over the aortic area. The pulmonic second sound was accentuated. The apical rate was counted as 132, while the radial was counted as 108, both very irregular. The abdomen was distended, a definite fluid wave was present with dulness in either flank. The liver was palpated four fingers below the costal margin, and very tender. The splenic edge was not palpated. There was a complete loss of sensation of the right leg and foot, a marked discoloration of the toes, and a bluish mottling of the leg. The thigh was cool and cyanosed. There was no pretibial edema. The pulsations in both popliteal dorsalis pedis and posterior tibial arteries were absent. The femoral pulsation was absent on the right side (Fig. 157). Within a few days the left leg became blue and cold, and sensation was diminished when tested with cotton-wool and pin-point. The left foot finally became gangrenous, and the thigh was blue and cold (Fig. 157). The knee reflexes remained active. The pain in the legs was severe and prevented sleep. A diarrhea started, the patient gradually grew weaker and died fourteen days after admission, with no necropsy permit. An opinion was expressed as that of chronic rheumatic endocarditis with mitral stenosis, auricular fibrillation, and myocardial insufficiency, complicated by a Rider's embolus and thrombus at the bifurcation of the abdominal aorta.

THE CLINICAL PICTURE OF EMBOLISM AND THROMBOSIS OF THE ABDOMINAL AORTA

Before discussing symptomatology we wish to say a few words in differentiating between embolism and thrombosis of the abdominal aorta. Welch[47] states that it is difficult to infer from the published descriptions how many cases were due to embolism and how many were due to thrombosis. However, he divides his 59 cases as 45 referable to embolism and 14 to thrombosis, the ratio being about three to one. Hesse[15] and Wylde[45] also believe that embolism is the more common. The sudden appearance of symptoms and the presence of infarctions of the spleen, kidney, brain, lung, intestines, etc., associated with

abdominal aortic obstruction, seems to point strongly to the embolic nature of the aortic plug.

Symptoms of abdominal aortic obstruction may be divided into two types: first, those with a slow onset and, second, those with a sudden onset. In the slowly forming obstructions of the abdominal aorta, intermittent claudication has been described as an early sign by Mazoux.[27] As the obstruction enlarges, numbness, coldness, formication, pallor, and final gangrene of one or both lower extremities develops. With the onset of gangrene, usually severe pain, constant or paroxysmal, occurs. The extent of the gangrene depends upon the completeness of the obstruction and the adequacy of the collateral circulation. The plug may be so situated as to interfere with the circulation in the one leg more than the other and, therefore, the signs of mortification vary in the two lower extremities. Reflexes may be absent, impaired, increased, or normal. Sensory disturbance is nearly always present. It may be partially lost, or completely so. Paraplegia may develop. Pulsations of the vessels are absent or diminished.

It is believed by some that the slowly progressive obstruction of the aorta is more often associated with thrombosis. However, in by far the greatest number of instances the onset is acute. The patient is suddenly seized with a severe, sharp, intense, agonizing pain, referable in most instances to the lower extremities, and sometimes to the loins and abdomen. The pain may be constant, but is usually paroxysmal in character. Evidences of shock appear and the patient is covered with a cold, clammy perspiration. Soon after there occurs coldness, numbness, and complete absence of sensation over the parts involved. Paraplegia, complete or partial, sets in early. Marked tenderness over the affected part may be present. Sensory disturbance may extend up to the knee or Poupart's ligament, or even higher. After a short interval the extremities become cyanotic and finally gangrenous, the extent of gangrene varying with the degree of blockage and also the length of time the patient survives. The gangrene may be unilateral, but more often is bilateral. Edema is usually absent. Of greatest diagnostic

importance is the absence of pulsation in the arteries of the lower extremities from the femorals down. The pulsation may be lost at the same time in both extremities, or first in one and then in the other. The reflexes may be diminished, absent, normal, or increased. In the 5 cases reported the knee-jerks were active in 3, absent on the others. Others symptoms, such as fever, vomiting, incontinence, and abdominal distension, occur within a few days. The pulse weakens and death occurs in the great majority of cases within a few days to several weeks.

The prognosis is always grave. However, survival from two to four years after the beginning of symptoms has been reported. Hesse,[25] in the 73 cases he collected, showed that 95 per cent. died under expectant treatment, and in only 10 cases was an attempt made to remove the obstruction. One case lived two and a half years after an aortotomy with removal of the embolus. Bauer[4] reports the case of a male, thirty-nine, suffering with a rheumatic mitral stenosis and insufficiency, with an irregular pulse, who suddenly developed signs of embolism of the abdominal aorta. He was operated within three hours of the onset.

The abdominal aorta pulsated to within 3 cm. of the bifurcation. The rest had no pulsation. The clot was palpated, extending into both iliacs. The embolus, 3 cm. long, shaped like a tooth with two roots, crown being at the aorta and the roots in the iliacs, was easily removed. After which the pulsation returned in both lower extremities, and the patient was discharged thirty days after admission, with no evidence of obstruction. However, in a number of cases in which embolectomy was performed, a fatal issue was the result: Hesse,[15] 2 cases; Lundblad,[26] 2 cases; E. Key of Stockholm,[19] 6 cases (quoted by Huisman[17]); Turreti and Guder,[44] 1 case.

The presence of recognized cardiac disease, particularly mitral stenosis complicated by an auricular fibrillation, with the history of sudden pain in the lower extremities followed immediately by changes in color and temperature of the skin, with a paraplegia following, the absence of pulsations in the blood-vessels from the femorals down indicates unmistakable obstruction of the arterial supply of those extremities, and it is recognized that such an ob-

struction is most always located at the bifurcation of the abdominal aorta. In the slowly progressive occlusion of the abdominal aorta where the symptoms are slow in their manifestations, there may well be some difficulty in arriving at a correct conclusion, but eventually the clinical picture is quite similar to that of the acute obstruction and the diagnosis becomes apparent.

As the great majority of cases of occlusion of the abdominal aorta are in association with cardiac disease, the treatment is twofold. First, treatment of the cardiac disease and, second, treatment of the aortic obstruction. As to the treatment of the underlying cardiac condition, little need be said here. For the treatment of the actual occlusion there are two methods. First, one can immediately massage the area, hoping to dislodge the clot and localize the obstruction in one extremity or both (Aubertin[2]). This procedure may require an amputation later. If the first fails, the second method, namely aortotomy, can still be resorted to and, if successful, offers a better prognosis than the non-surgical treatment, as amputation may be required in the former. To be sure of any degree of success, the operation should be performed early. In the case operated successfully by Bauer, it was done three hours after obstruction, and the case, reported by Hesse, that was operated successfully and lived two and a half years, was done within twelve hours of the obstruction. Therefore, the important point in treatment is an early diagnosis, with an immediate attempt to remove the clot. Cases coming under observation where operative interference is impossible, the treatment is symptomatic, morphin in large doses to relieve the pain, heat locally, and cardiac stimulation, but in this type a fatal outcome is almost certain.

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CARCINOMA OF THE ESOPHAGUS. WITH REPORT OF FOUR UNUSUAL CASES

THE subject of carcinoma of the esophagus has been so completely and thoroughly covered in the literature, especially by Chevalier Jackson, that it would be presumptuous for me to add my small contribution but for the fact that it is today an almost invariably fatal disease, practically never recognized until it is too late even to modify its fatal course. Such a subject requires emphasis, not only to encourage earlier diagnosis, but also to stimulate research tending to find a cure; and cure in esophageal carcinoma, owing to its inaccessibility, will depend, more than in probably any other type of carcinoma, on the discovery of some universal carcinoma cure, some substance which, when injected into the body, will dissolve out carcinoma tissue wherever found, leaving healthy tissues intact. This paper will present briefly an analysis of 38 cases of esophageal carcinoma seen by me in the past five years.

Pathology.—Carcinoma occurs in the esophagus in the form of several types of tissue. Epithelioma is the common type occurring primarily in the esophagus, and in our 38 cases, epithelioma was found in 22 cases, or 58 per cent. The seat of the primary lesion was in the upper end of the esophagus five times, in the middle portion five times, and in the lower end twelve times (Table I). Adenocarcinoma involving the lower end of the esophagus, as an extension from a primary gastric carcinoma, was found in 12 cases, or 31 per cent. There was also 1 case of adenocarcinoma primary in the upper third of the

esophagus, originating in the islands of mucous glands resembling gastric glands, which are occasionally found in the upper third of the esophagus, a type described by Ewing and others.

TABLE I. CARCINOMA OF ESOPHAGUS

ANALYSIS OF 38 CASES

Location	Number of cases.	Type: Epithelioma.	Adenocarcinoma.	Not determined.
Upper third	6	5	1	..
Middle third	5	5	..	..
Lower third, involving stomach	16	3	11	2
Lower third, not involving stomach	11	9	..	2

Etiology.—Of our group of 38 cases, 31, or 81 per cent., were males, and 7, or 19 per cent., females (Table II). The average age of onset was 55.6 years, the oldest patient being seventy-three years of age, the youngest, thirty-seven years. Although careful histories and routine Wassermann tests (in blood, and often in spinal fluid), were done in all cases, only 1 patient was found to be syphilitic, his case being 1 of the 4 described below. A definite history of alcoholism was obtained from 15 patients, or 40 per cent., suggesting irritation from alcohol as being an etiologic factor to be seriously considered. Every patient in the series showed definite evidence of oral sepsis, 3 having had all teeth recently extracted, and many exhibiting some of the worst cases of pyorrhea ever seen in our clinic. Oral sepsis may play an important part in the etiology of this disease. A history of the habitual drinking of too hot liquids, often mentioned as a possible contributing cause, was not obtained any more frequently in this series than in any other average group of individuals, and I doubt whether it has any bearing in the etiology of this disease.

TABLE II. CARCINOMA OF ESOPHAGUS

ANALYSIS OF 38 CASES

Sex	Male 31 = 81 per cent.	Age	Average 55.6 years
	Female 7 = 19 "		Highest 73 "
			Lowest 37 "

Symptomatology.—The principal symptoms of esophageal carcinoma are pain, dysphagia, and regurgitation. Preceding these esophageal symptoms there may be a hardly noticeable period of fairly short duration, during which the patient notices a gradual loss of weight and strength, and a vague sense of uneasiness or moving or "lump" in the epigastrium or along the line of the esophagus, coincident with or independent of swallowing. The definite esophageal symptoms are caused by several factors. Due to the narrow lumen of the esophagus, even a small growth will begin to cause some *obstructive symptoms* early, probably beginning as a localized or, at times, a more distant, reflex *spasm*. This accounts for the occasional early symptom of intermittent sudden regurgitation of food immediately after attempting to swallow, caused by upper esophageal or cricopharyngeus spasm, even though the growth may be much further down the esophagus, even at the cardia.

TABLE III. CARCINOMA OF ESOPHAGUS

ANALYSIS OF 38 CASES

Location.	Number of cases.	Initial symptom:		Averaged duration (mos.):	
		Dysphagia.	Pain.	Dysphagia.	Pain.
Upper third	6	5	1	4	5
Middle third	5	2	3	7	10
Lower third:					
Adenocarcinoma	11	3	8	7	$9\frac{1}{2}$
Epithelioma	12	7	5	4	$5\frac{1}{2}$

The *true dysphagia* of malignancy starts mildly and is progressive, as distinguished from the intermittent, complete dysphagia due to spasm. In our 38 cases a history of dysphagia was obtained in 32, the average duration of this symptom being 4.25 months before admission. There is noticed at first a moderate difficulty in swallowing solids, especially bread and meat, though often, when stuck, they can be pushed through with a drink of water. Over a period of a few months the patient notices increasing difficulty with solids, then soft foods, and finally liquids, obstruction to liquids occurring in our series in from two to nine months from the onset of obstructive symptoms. In the early stages of the obstruction the patient

may not realize that his difficulty is in swallowing, but may describe a "sticking feeling" after eating. As the location at which this symptom occurs usually corresponds pretty closely to the actual location of the growth, lower esophageal lesions, causing epigastric or lower sternal symptoms, will often be considered as being of gastric origin, but if carefully questioned even a very ignorant patient will describe the feeling of food sticking there on swallowing. With increasing obstruction, *regurgitation* of food will occur, earlier in upper than in lower esophageal lesions. Although, especially when occurring early, it will be described by the patient as "vomiting," true regurgitation can usually be distinguished from vomiting by the fact that the food is returned unchanged in taste and appearance, milk not being curdled except in the rare cases of incomplete lower esophageal obstruction, in which some gastric juice may be regurgitated into the lower esophagus. Only 1 of our 38 patients noticed regurgitation as the first symptom of his disease.

Pain in the lower sternal or epigastric regions was complained of in 32 of our 38 cases, its average duration being nearly twice as long as that of dysphagia, namely eight months. This would make it seem that a history of pain might be a very valuable early diagnostic aid, but on studying the character of the pain complained of it is noted that it was of such an indefinite character that it would not have led to a suspicion of an esophageal lesion until dysphagia supervened. Though frequently occurring with swallowing, the pain was often steady, a feeling as of some heavy and frequently only mildly painful lump in the lower sternal or high epigastric regions. With the occurrence of dysphagia the relation of the pain to swallowing was first noted. A study of Table III will show that pain is more frequently the initial symptom in lower esophageal adenocarcinoma, which has originated in the stomach, dysphagia in the primary epithelioma of the lower esophagus. In upper and middle esophageal lesions, dysphagia and pain divide the honors evenly as initial symptoms. In 2 of our patients pain had been present for several months, and the dysphagia came on suddenly after an alcoholic debauch.

The general symptoms of carcinoma, cachexia and the loss of weight and strength, are accentuated in esophageal lesions by the fact that the patient gradually undergoes an enforced starvation. In our series the loss of weight varied from 20 to 80 pounds, and averaged over 40 pounds, the weight loss, though occasionally preceding the onset of local symptoms, being particularly rapid after the onset of the dysphagia.

Bleeding is usually present, but is more frequently a surface oozing rather than a frank hemorrhage. Only 5 of our 38 patients gave a history of hematemesis, though a considerable number described regurgitation of blood-streaked esophageal contents.

Cough is a frequent accompaniment of esophageal obstruction, and is often due to aspiration into the bronchi of food or infective material regurgitated from the esophagus. Bronchitis is often caused by this aspirated material, and terminal bronchopneumonias may, in part, also be due to this factor. In our series we had 1 case of multiple lung abscesses, giving at autopsy the appearance of abscesses caused by the breaking down of metastatic nodules. The hard, brassy cough and husky voice, typical of vocal cord paralysis from recurrent laryngeal nerve involvement in the growth or glands, is more common in upper esophageal lesions. Five of our patients had this complication.

Diagnosis.—The diagnosis of esophageal carcinoma can usually be made from the symptoms alone—a gradually increasing dysphagia, regurgitation of food, lower substernal pain, and rapid emaciation in an individual past thirty-five or forty years of age being practically pathognomonic of this disease. It is unfortunate that so many patients are permitted to reach the advanced stage of the disease indicated by these symptoms before a diagnosis has been made, or even a suspicion entertained as to the nature of the lesions. And yet most of the patients reaching the larger clinics have had such well-marked symptoms for months before admission, no one apparently having taken the time to get a history. If anything is ever to be done for carcinoma cases it is going to be done for the very early lesions,

although in esophageal carcinoma there is as yet no infallible cure at any stage.

Early diagnosis must depend to some extent on surmise. The early symptoms of vague discomfort along the line of the esophagus, associated with a moderate loss of weight and strength, and increasing pallor, especially in individuals of carcinoma age, should occasion a suspicion of carcinoma, and should be the indication for a thorough diagnostic survey. Several methods of diagnosis are available, and will be described in the order of their usual employment.

Passage of a stomach tube, the ordinary soft, flexible tube of No. 28 to 35 F. size, will be interrupted at a point of obstruction or spasm in the esophagus. If the obstruction is only partial, firm pressure will push the tip of the tube through the narrow area, the tightness and smoothness of which will be fairly definitely perceptible to the examiner's fingers. In spasm, firm pressure may cause the tube suddenly to "drop through" the point of constriction, with no more resistance encountered for some distance. On withdrawing the tube, a blood stain on the tip will indicate ulceration at the point of constriction, which usually means carcinoma. The possibility of doing damage by means of the stomach tube is rather remote, but the passage blindly of any stiffer tube, such as a bougie or esophagoscope, must not be attempted until the *x*-ray has shown that there is no aneurysm of the aorta which might be ruptured, and no thin wall or diverticulum which might be perforated. The earliest diagnosis ever made by me, in a case having a carcinomatous nodule the size of one-half of a split pea, causing no obstructive symptoms, was prompted by the observation that a Rehfuss tube, passed preliminary to a routine fractional gastric analysis, would not enter the stomach for over one-half hour, even with the aid of a drink of water, although a large stomach-tube passed through into the stomach easily. The tip of the Rehfuss tube was blood-stained, whereas the large stomach-tube was clean. Obstruction to the passage of either type of tube, temporarily or permanently, should, therefore, be the signal for further study.

The *Roentgen ray* has proved to be a great aid in diagnosis. In the earlier lesions, with little or no real obstruction, careful *fluoroscopy* will often reveal slight temporary delay in the passage of a swallowed barium mixture at some point where such delay is not normal. The use at first of a barium sulphate and water suspension meal may disclose some barium adherent at the point of ulceration, but for detecting the earliest possible lesions a thick barium sulphate and cereal or gelatin mixture is the best. Even this thick mixture will at times pass an early lesion uninterrupted, whereas capsules of varying sizes, filled with plain barium sulphate, may be held at some point of even very slight spasm, indicating a possible lesion at that point or below. Radiograms of the esophagus can be very satisfactorily obtained if the patient is made to lie on the table in a sort of modified Sims position, so that the shadow of the esophagus will fall to one side of the spine and the lower end be elevated somewhat above the upper end. The patient then sucks a thick barium mixture into his mouth through a flexible rubber tube, and at a given signal swallows the mixture, the exposure being rapidly made as the barium mixture passes down the esophagus. By this method the use of sausage skin or rubber bags passed down into the stomach, and filled with an opaque mixture, can usually be obviated, as beautiful films of the entire esophagus can be made. Constant irregular defects or irregular, chewed-out-looking obstructive outlines are characteristic of malignancy, but the rather rare, non-ulcerative type of cancerous lesion may show a smooth defect or obstruction. Often the outline of the tumor can be traced as an area of increased density, outside the esophagus, surrounding the region of the defect. An occasional source of error in *x*-ray diagnosis is the finding of a cardiospasm in cases of carcinoma of the cardiac end of the stomach. Carcinoma in this region is probably more frequently overlooked than in any other part of the gastro-intestinal tract, due to the fact that in erect fluoroscopic examination the cardiac end of the stomach is never completely filled and, in the usual prone pictures, is merely indicated by the presence of the "Magenblase." Careful study of the barium outline

as seen in this gas-bubble, and films taken in the supine position, will often disclose the characteristic irregular defect of carcinoma. A complete gastro-intestinal *x*-ray series should be done in all patients with alimentary tract symptoms, even though an esophageal lesion is found, as the findings further down in the tract may materially affect the decision in regard to treatment of the esophageal condition.

Esophagoscopy, in the hands of an expert in this form of examination, is the only sure means of making a definite diagnosis of esophageal lesions. In my clinic we turn this work over to the endoscopist of the otolaryngological department. This procedure not only gives the examiner the opportunity of inspecting the entire inner surface of the esophagus, but permits of the removal of specimens for microscopic examination. Practically all observers are now convinced that the removal of such biopsy specimens is attended with little or no risk to the patient. Even without removal of specimens, the finding of an irregular, nodular, ulcerating area in the esophageal wall or protruding into the lumen at the cardiac end of the stomach is practically pathognomonic of carcinoma, although the extremely rare peptic ulcer of the esophagus may give a similar appearance, and an occasional malignant tumor will disclose a smooth outline. If a spasm is encountered at any point, attempts may be made to relax it by the topical application of saturated magnesium sulphate solution (Meltzer's suggestion), or by the passage through the esophagoscope of a flexible rubber obturator, but the attempted forcible passage of the esophagoscope through such an area of resistance may be attended with perforation of the esophageal wall. If passage of the tube through the spastic area is successful, the presence or absence of a malignant lesion below this point may be definitely established, but it is better to put off the making of this definite diagnosis until a later time than to subject the patient to the risk of perforation by undue haste.

Perforation of the esophagus by the esophagoscope is attended by rather mild symptoms at first, except in the cases of upper esophageal perforation, in which a subcutaneous emphysema rapidly supervenes. In 2 cases seen by me, this emphysema

extended entirely around the neck, upward into the face, and downward over the chest wall for some distance. There seemed also to be extravasation of air in the deeper tissues in the mediastinum and upper thorax. The condition subsided in 1 case inside of twenty-four hours, in the other it lasted for three days, but in both cases was unattended by any other alarming symptoms. The patient whose emphysema subsided after three days apparently had no ill-effects from his perforation, but the other patient died after twelve days, apparently from an infection, although unfortunately an autopsy was not obtained. Perforation of the lower end of the esophagus is usually not noticed at the time of the examination, in fact, I believe that occasionally infection of the esophageal wall by the removal of a biopsy specimen may be the starting point for a slow perforation, symptoms of which will not develop until later. In 2 cases afterward seen by me there was no shock and no fever, but after nine and eleven days respectively, there occurred a febrile reaction with temperatures to 104° F., pulse to 120, and respirations no higher than 25. Both patients died fourteen days after the esophagoscopy and autopsy revealed linear abscesses, extending alongside the esophagus for some distance below a very small perforation. Aside from the rather localized necrotic areas there were no evidences of a spreading infection, although mild bronchopneumonia was present, but it seemed as if the patients' lowered resistance to infection, due to the prolonged starvation and cachexia, had prevented their successful coping with the situation. One case of perforation developed fever, cough, and pain in the chest the day after esophagoscopy, and died on the tenth day when perforation of the aorta occurred. All the patients who were perforated had extensive carcinomatous involvement.

Complete physical examination is, of course, indicated in all patients with esophageal symptoms, and the finding of glandular involvements, metastases, and coexistent tuberculous, syphilitic, or other manifestations might greatly modify the therapeutic procedures in a given case. Moderate leukocytosis, 12,000 to 14,000, was present in 50 per cent. of our cases.

Clinical Course.—An untreated case of esophageal carcinoma will have an increasing obstruction to the passage of food, until even liquids cannot be swallowed. At this stage, death from starvation and toxemia may occur or, after a period during which no attempt at swallowing is made and irritation of the malignant area is thus avoided, there may be some remission in the size of the tumor mass and swallowing may again be possible. Aspiration of esophageal contents or perforation into the bronchi may cause pneumonia or lung abscess, spontaneous perforation into the aorta may cause sudden death, or metastases into mediastinum, lungs, liver, or other abdominal organs may be the ultimate cause of death.

Treatment.—The treatment of esophageal carcinoma is mainly palliative. In spite of the optimism of the surgeons who have attempted complete surgical extirpation of the full thickness of the esophageal wall well beyond the carcinomatous involvement, but 2 cases have survived long enough to be called cures. And yet these 2 are the only cases of cure of the esophagus on record in which a cure has been accomplished by any of the means at hand. Operation is, of course, impossible in the lower esophageal growths whether secondary to gastric malignancy or not, and removal of the extreme upper end of the esophagus is also manifestly impossible. The difficulties attendant upon operative removal of any part of the esophagus are obvious.

Radium therapy, either by means of emanation tubes introduced into the lumen or emation needles inserted into the growth, while causing subsidence or entire disappearance of the local lesion, has not prevented death from metastases, cicatricial contraction, or from perforation. It can be classed only as a palliative measure, and after many years' experience with this method of treatment, dating back to a considerable number of cases treated as far back as fifteen years ago by Dr. Henry H. Janeway, a pioneer in this form of therapy, I do not believe that the slightly beneficial results obtained from radium treatment justify the risks involved or the subjecting of a patient to the terrific reactions which always follow the treatments.

The results from deep *x-ray therapy* are no more satisfactory and no less distressing than those from radium.

The opinions regarding the most satisfactory *palliative treatment* vary considerably. The exponents of *gastrostomy* advise that it be done early, and point out that if done in a still fairly well-nourished patient it may prolong life for a considerable length of time before the patient dies of metastases. My experience has been that, even in cases where an almost ideally functioning gastrostomy stoma has been produced and where mouth hygiene and esophageal lavage have taken care of the distressing upper esophageal symptoms, the patient's mental reaction to the tube feedings and to the evidently increasing weakness and emaciation has been such that the operation has been a regret to all concerned.

Medical palliative treatment consists in soothing the irritated, ulcerating surface by rest, by the administration of oils, and by the feeding of highly concentrated, soothing liquid mixtures. In cases of nearly complete obstruction, a few days of esophageal rest, with rectal and intravenous injection of glucose solution, together with a cleaning up of the mouth and the washing out of the throat and upper esophagus with normal saline or mildly alkaline solutions, will usually result in a subsidence of the edema and inflammation of the mucosa over the growth, and will permit of the feeding of mixtures of milk, cream, lactose, egg, and often of thin cereal gruels. Occasional periods of rest are indicated. The introduction through the constricted area of tubes of various kinds, as suggested by many authors, is usually not necessary, but may be a help in some cases. Dilatation of the esophagus at the point of obstruction, while always attended by the risk of perforation, is often worth while, and the method of choice is by means of the passage of an esophagoscope. Blind bougienage is much more dangerous, but where dilatation must be frequently performed is more comfortable for the patient. Pain must, of course, be controlled by sedatives, but where the patient co-operates in regard to diet and mouth hygiene, the final stages of this disease are often not as distressing as in cases of carcinoma elsewhere.

SUMMARY

1. Carcinoma of the esophagus is frequently not recognized till far advanced.

2. The early symptoms are mild and indefinite.

3. Early diagnosis is possible only by means of the esophagoscope.

4. The treatment is essentially palliative, though operation may be attempted in early cases.

REPORT OF UNUSUAL CASES

Case I.—E. B., male, married, American, miller, sixty-one years old, was admitted to the Long Island College Hospital October 21, 1926. His family history was negative. He had had diphtheria and scarlet fever as a child, but no other acute infectious diseases. He had been married twenty-five years, his wife was healthy, and had had four healthy children. Venereal history denied. He had used alcohol moderately. Eight months before admission, he had begun to have a fulness and burning in his throat and under upper sternal region, increased by deglutition. Under home treatment there had been an increasing dysphagia and pain for four months, at which time, after esophagoscopy, he had received some dilatations at Kings County Hospital, and for eight weeks afterward had swallowed better. For six or eight weeks before admission there had been again an increasing dysphagia, and on admission he was swallowing liquids with difficulty. He had lost 60 pounds in weight.

Examination.—Marked emaciation and dehydration. Face florid. Teeth: markedly pyorrheic. Nose and throat: not infected. Heart and lungs: negative. Blood-pressure: 120/70. Abdomen: slightly distended, muscles held rigid, liver enlarged, hard, irregular in outline. Sense of resistance high in epigastrium. Reflexes: normal. Supraclavicular and inguinal glands enlarged. Wassermann: negative in blood and spinal fluid, the latter being negative in all other respects. Blood-count: red blood-cells, 4,000,000; white blood-cells, 8800; hemoglobin, 78 per cent. Differential, normal. Icterus index, 3.6. Van den Bergh, positive indirect. Blood-culture, sterile. Urine, negative. Tem-

perature, low febrile course, ranging from 99° to 101° F., except for last few days when it reached 102° F. Passage of stomach tube, 32 Fr., was interrupted at 8 inches from teeth, the patient indicating that this was the point of obstruction to swallowing. Fluoroscopy showed no evidence of aneurysm and no medias-

Fig. 158.—Adenocarcinoma of esophagus (primary).

tinal enlargement. The barium paste was regurgitated quickly after initial act of swallowing, so that it did not remain in esophagus long enough for filming. The opinion was that there was extrinsic pressure on upper esophagus.

Esophagoscopy, by Dr. Harry Meyersburg, showed obstruction 8 inches from the teeth (just below the entrance to the

esophagus). There was no evidence of mucosal involvement, so that no specimen could be removed.

Under the usual symptomatic care the patient grew gradually weaker, and died in three and a half weeks.

Autopsy by Dr. Archibald Murray showed a carcinomatous esophageal mass, extending downward 10.5 cm. from the beginning of the tube, and invading the trachea for a distance of 4.5 cm. The growth was 2 cm. in width (Fig. 158). The stom-

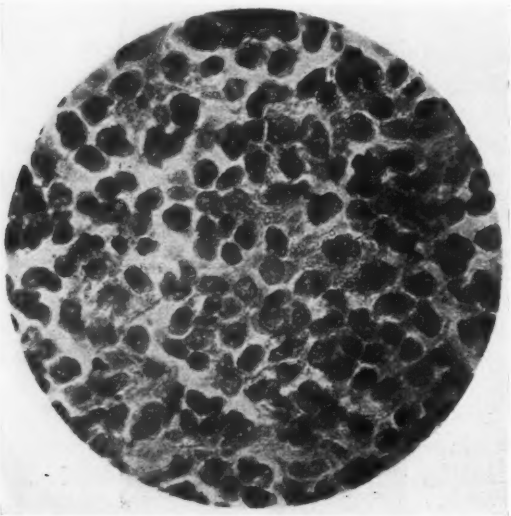

Fig. 159.—Adenocarcinoma of esophagus (primary).

ach showed a tumor 3 by 4 cm. in diameter, on the greater curvature, near cardia. The liver showed a large tumor, occupying one-half of the liver. There were nodules throughout both lungs. The pancreas showed excessive connective tissue. Kidneys and spleen congested. Adrenals, negative.

The tumor of the esophagus had not eroded, but projected above the surface and was of polypoid type. The cells were not squamous, but were small, with not much protoplasm and of an indefinite type. An attempt at gland formation was seen

(Fig. 159). The same tumor-cells were seen in lungs, stomach, and liver.

Discussion.—This was a rare type of tumor, adenocarcinoma arising in the anomalous attempts at gland-formation occasionally occurring in the esophageal wall.

Case II.—H. K., male, single, American, engineer, seventy-two years old, was admitted to the Long Island Hospital, Febru-

Fig. 160.—Diverticulum of esophagus with carcinoma.

ary 16, 1926. His family history and general previous history were negative. For fifteen years he had had intermittent dysphagia, with diagnosis of esophageal diverticulum made from symptoms twelve years before. He had been able to take care of attacks of dysphagia by posture and auto-lavage until about six weeks before admission, since which time the dysphagia had been persistent and increasing. He had been unable to swallow even liquids for two days before admission.

Examination.—Marked emaciation and dehydration. Teeth,

all missing. Nose, throat, and ears, negative. Lungs, negative. Heart sounds weak, regular, no murmurs. Abdomen: wide, not tender, no masses palpable. No glandular enlargements. Reflexes, normal. Blood Wassermann, negative. Blood-chemistry, marked nitrogen retention. Blood-count, moderate

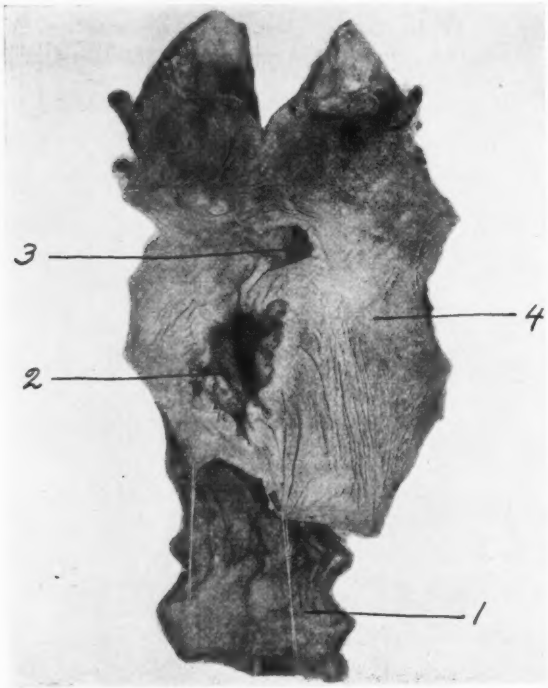

Fig. 161.—Diverticulum of esophagus with carcinoma. 1, Esophagus; 2, carcinoma—perforation into diverticulum; 3, neck of diverticulum; 4, smooth wall of diverticulum.

anemia. *x*-Ray showed typical upper esophageal diverticulum, with oblique films showing marked irregularity of esophageal wall at upper end of the diverticulum (Fig. 160).

Esophagoscopy by Dr. Harry Meyersburg showed an irregular tumor-mass just below the entrance to the esophagus,

below and to right of which there could been seen the diverticulum, the wall of which seemed to be involved in the tumor mass. A biopsy specimen was removed and showed epithelioma.

The patient died in three days, gastrostomy having been objected to.

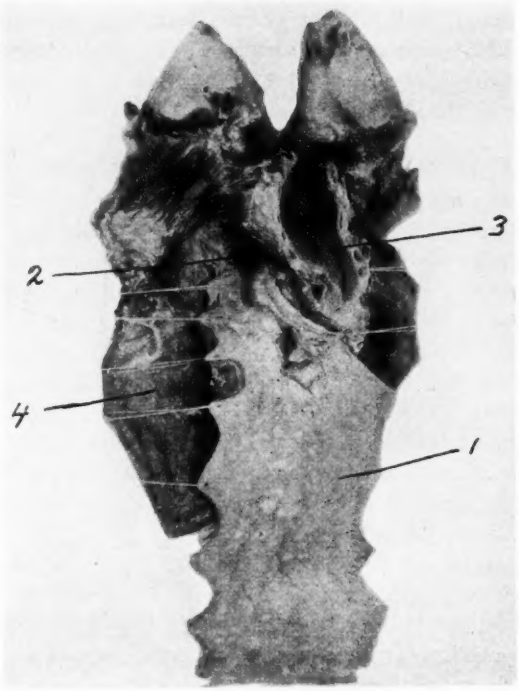

Fig. 162.—Diverticulum of esophagus with carcinoma. 1, Esophageal wall; 2, perforation due to carcinoma; 3, opening into diverticulum; 4, rear view of diverticulum.

Autopsy by Dr. Archibald Murray showed a large esophageal diverticulum just below the epiglottis. In this diverticulum was a smaller pouch with indurated edges and a wall made up of carcinomatous tissue. At a point about 5 cm. below the first ring of the trachea this smaller pouch communicated with

the esophagus through a necrotic opening. The esophagus entered the diverticulum high up. The tissues behind the first 5 cm. of the trachea were made up of tumor masses, which caused distortion and contraction of the esophagus (Figs. 161, 162). No other metastases found. Remainder of autopsy negative.

Discussion.—This was a case of long-standing esophageal diverticulum, with invasion of the diverticular and esophageal walls with epithelioma and perforation from lower end of diverticulum into esophagus, making two openings between esophageal lumen and the diverticulum.

Case III.—A. P., male, single, Norwegian, painter, fifty-eight years old, was admitted to the Long Island College Hospital, October 21, 1926. His family history was negative. He had a history of chronic alcoholism, had had a venereal sore fifteen years before, and had never been otherwise ill. Six weeks before admission he had begun to have epigastric and transverse upper abdominal pains constantly, but worse at night, often keeping him awake, not affected by food or defecation. For five weeks he had been having an increasing dysphagia, beginning with solid foods, but even water was swallowed with difficulty on admission. He had had no digestive symptoms, and his bowels had been regular until the present symptoms. There had been a loss of 50 pounds over a period of a few months.

Examination.—Marked emaciation and dehydration. Teeth, pyorrheic, with many carious stumps. Tonsils, small. Nose, not obstructed. Heart and lungs, negative. Blood-pressure, 122/55. Abdomen: narrow, scaphoid, indefinite sense of a mass high in the epigastrium. Cervical and inguinal glands, palpable. Pupillary reflexes, normal. Knee-jerks, sluggish. Romberg, questionable. Wassermann negative in blood and spinal fluid, the latter being also negative in all other respects. Urine, negative. Blood: red blood-cells, 2,900,000; white blood-cells, 8400; hemoglobin, 65 per cent.; differential, normal. Temperature: low febrile course, usually 99° to 100.4° F., with high point once at 102° F. Blood-cultures, sterile. Passage of stomach tube, No. 32 F., was interrupted definitely at 18½ inches from

teeth, with no blood on tip. *x*-Ray, delay but no obstruction in lower esophagus. Constantly irregular outline of posterior stomach wall in region of cardia, with six-hour retention of barium in this region—forty-eight-hour appendix residue (Fig. 163).

Esophagoscopy by Dr. Harry Meyersburg showed a stiffening of esophageal wall about the cardia, and so much spasm that the instrument could not be introduced into stomach. No

Fig. 163.—Epithelioma of esophagus and stomach.

ulceration or blood was observed. The patient was given rectal feedings, but he failed rapidly and the mass in his epigastrium could be felt more distinctly. He had a continued fever, showed moderate upper abdominal rigidity, and died twenty days after admission.

Autopsy by Dr. Archibald Murray showed pulmonary tuberculosis with caseation in both lungs, and a mass, size of peach, apparently arising in pancreas, adherent to posterior

stomach wall and esophagus and causing almost complete closure of the cardia (Fig. 164). There was no erosion of mucosa over tumor mass, but there was a linear abscess between the aorta and esophagus on left side, beginning three inches above cardia and apparently extending into the tumor mass.

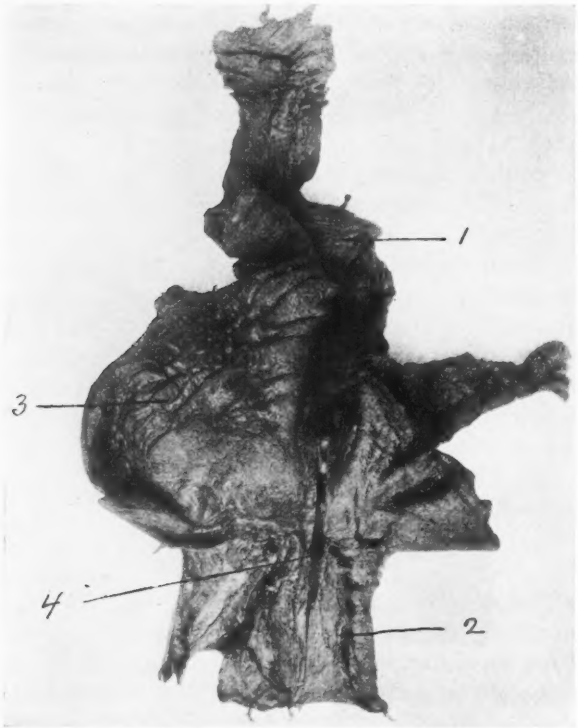

Fig. 164.—Epithelioma of stomach and esophagus. 1, Esophagus; 2, stomach; 3, mass (pancreas and growth); 4, cardia (sections removed).

Microscopic sections showed the pancreas to be invaded by large masses of squamous cells, with pearls. The stomach was not invaded, but after repeated sections of the esophageal wall there was finally disclosed epitheliomatous involvement, though very slight. There was slight atheroma of aorta, with several

foci of tumor-cells in adventitia. Lymph-nodes also showed tumor-cells.

Discussion.—This was a case of lower esophageal epithelioma, with very slight esophageal involvement and no ulceration, but with a large metastasis into pancreas, and involvement of lymph-nodes and aorta.

Case IV.—C. M., male, widowed, American, burnisher, forty-nine years old, was admitted to the Long Island College Hospital, January 19, 1926. His family history was negative. He had had diphtheria as a child, a chancre eighteen years, and rheumatic fever twelve years, before admission. His wife had died of tuberculosis. He had been a steady drinker of wine and beer, but had never had any gastro-intestinal disturbances until four weeks before entering hospital, when, following the drinking of undiluted gin, suddenly he experienced an inability to swallow solids or liquids. After four days there was a sudden cessation of the obstruction, followed by a gradually increasing dysphagia until three days before admission he again was unable to swallow anything, food seeming to stick in upper sternal region and returning unchanged into mouth, accompanied by much glairy mucus.

Examination.—Moderate emaciation and dehydration present. Pupils irregular, reacted slightly to light. Conjuctiva, reddened. Teeth, severe pyorrhea, many caps, bad caries. Throat, edematous and reddened, with postnasal drip visible. Paralysis of left vocal cord. Heart, auricular fibrillation. Blood-pressure, 112/78. Lungs, negative, except for slight emphysema. Abdomen: scaphoid, not tender, liver palpable just below rib margin, sense of resistance high in epigastrium. Glands, epitrochlear and inguinal, shotty. Reflexes, knee-jerks present, no Babinski, no Romberg. Blood-count, normal. Wassermann, negative in blood and spinal fluid. Spinal fluid: Colloidal-gold curve, negative; globulin, 3+; Fehling's, 2+; cell count, 5. Urine, negative, except for few granular casts. Temperature: low febrile course, from 99° to 101° F., except for the last two days, when it reached 105° F.

Passage of stomach-tube, No. 32 F., was interrupted at about 30 cm. from teeth, no blood being seen on tip on withdrawal.

Fluoroscopy and films (Fig. 165) showed smooth obstruction at junction of upper and middle thirds of esophagus. Barium meal passed in thin stream through to stomach, and remainder of gastro-intestinal tract was negative, except for colonic hypermotility.

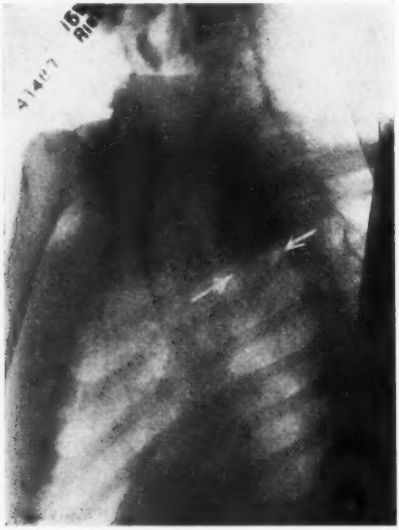

Fig. 165.—Epithelioma of esophagus, associated with syphilis.

Esophagoscopy (January 21st) by Dr. Harry Meyersburg, showed a mass about 12 cm. below the esophageal mouth, pale, smooth, not ulcerative, and appearing like an extrinsic mass, causing pressure against the esophagus.

With these findings, and a history of an old chancre followed by *only* two weeks' treatment, the patient was given intensive syphilitic treatment. His esophagus opened somewhat after the esophagoscopy, and he was given a high-caloric liquid and semi-liquid diet. In two and a half weeks, esophagoscopic

findings were the same as before. On February 19th, one month after admission, esophagoscopy by Dr. Harry Meyersburg showed a mass on anterolateral wall, extending 8 cm. down from a point 24 cm. from the teeth. Biopsy specimens were removed and showed epithelioma. The day following this examination the patient went into shock, and a marked dulness appeared over mediastinum and right base, with breath-sounds markedly

Fig. 166.—Epithelioma of esophagus. 1, Tumor mass; 2, glass rod in fistula.

diminished over both lung-beds. His temperature rose to 105° F., and he died about forty-eight hours after the esophagoscopy.

Autopsy, performed by Dr. Vance, showed a growth, 7 cm. long, beginning at about 4.5 cm. below the upper end of the esophagus. The surface was ragged and necrotic, and at the lower end there was communication with a fistula running down along the outside of the esophagus almost to the stomach

(Fig. 166). This fistula was necrotic, and full of pus and broken-down tissue. Microscopic sections showed typical epithelioma tissue in the tumor and in neighboring lymph-nodes. The lungs showed catarrhal pneumonia, the liver, stomach, and pancreas were negative, and kidneys showed some congestion.

Discussion.—Carcinoma in a syphilitic is often confusing, but intensive treatment is indicated to make a diagnosis. This tumor was unusual in that it did not ulcerate early. Perforation was probably done at time of second esophagoscopy, about ten days before death.

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TOXIC HEPATITIS AND HEPATOLYSIS FOLLOWING THE USE OF ATOPHAN

ACUTE yellow atrophy of the liver has been noted by many observers to be on the increase. Women are more frequently attacked than men. Most cases occur in the earlier decades of life. It has been found to occur in various infections, toxemias, and intoxications. The list is long and varied. The spirochetæ of syphilis and Weil's disease, typhoid and paratyphoid bacilli, Bacillus coli, influenza bacillus, and the gonococcus, have all been implicated. Acute yellow atrophy has been noted to follow erysipelas, skin abscesses, septic gangrene of the foot, suppurative meningitis, osteomyelitis, appendicitis, salpingitis, sepsis,* pneumonia, and diphtheria. Mushrooms (Amanita phalloides), chloroform, phosphorus, dinitrotoluol (munition workers), HCN, single large dose of alcohol, picric acid, trichlorethane, dinitrobenzol, aspidium, theacylon, caseosan, and yatren have produced instances of this disorder. While arsenic rarely does so, salvarsan in all stages of syphilis and in non-syphilitic cases has been found to produce liver atrophy. Hyperthyroidism and toxemia of pregnancy may produce the same. Acute hepatolysis has been described by Ortel, and observed by the author in cases of severe cardiac stasis of the liver.

A few years ago it was thought that catarrhal jaundice might be a precursor of acute yellow atrophy. Today we believe that it is probably but a mild form of acute hepatitis which may go on to atrophy. Infectious cholangitis, due to Bacillus coli infection, is believed by some authorities to result in severe parenchymatous hepatitis. It is believed that intestinal infection may result in

* Hepatolysis may occur in any sepsis without the production of liver abscesses.

the formation of toxic products which can cause hepatolysis. Cases of acute yellow atrophy or a milder form of hepatitis have appeared in the literature, which are to be attributed to the use of atophan or its derivatives.

Atophan, chemically 2-phenyl-quinolin—4 carboxylic acid, introduced about a decade ago, is being used with excellent results in rheumatism, gout, gall-stones, and neuralgic states. As a rule, it may be given for a long time without any toxic results.

From time to time cases have been reported (Schelling[1]) where general pruritus, rashes (especially of the scarlatinal character), urticaria, angioneurotic edema, fever, headache, malaise, aphthæ of the mouth and pharynx, nausea, vomiting, diarrhea, bronchitis, and cardiac collapse have occurred. The writer has observed a very severe case of acute toxicity attended by marked stupor, angioneurotic edema, high fever, and oliguria following the ingestion of one $7\frac{1}{2}$-gr. tablet of atophan. Toxic jaundice and hepatolysis may occur not only from atophan (cincophen), but also related drugs such as atophanyl (a combination of sodium salt of atophan and salicylic acid) and diiodatophan (Biloptin is its trade-name, and consists of 50.7 per cent. iodin), which has lately been used in Germany and Austria for cholecystography because of its high iodin content.*

Brugsch and Horster[2] found that atophan was an irritant to the liver parenchyma. The toxic action is due to the quinolin nucleus, consisting of the benzene and pyridin rings which yield the toxic-free benzene-ring. It has been shown that toxic jaundice rarely occurs from the use of the inorganic arsenic or sodium cacodylate, but does occur after arsenobenzol (salvarsan) or trinitrotoluene, in either case being due to the contained

* The writer does not wish to discuss the cases of toxic jaundice following the use of atoquinal, which is a derivative of quinolin and not of atophan, and is an allylphenylcinchonin ester, also containing the toxic benzene-ring. W. Langdon-Brown[7] reports two fatal cases of toxic jaundice after atoquinol injections and states that he knew of several others. The injections had been given for rheumatoid arthritis. "The symptoms were similar to those in other hepatic toxemias arising from ring compounds." It was his belief that it was more than a coincidence.

benzene nucleus (Willcox[3]). It is highly possible that many cases of hepatolysis of unknown origin or thought to be of septic nature (where, because of associated joint or muscle or nerve pain, atophan had been given) may be directly ascribed to the previous use of atophan. Most individuals fortunately are not susceptible to the toxic effect of the drug. Toxic jaundice will only result in the presence of an individual idiosyncrasy. The dose, or duration of the use of the drug, will vary in the individual case—one developing toxic jaundice after a small dose, while another may not develop it until after repeated large doses.

Of greatest importance is probably the amount of glycogen storage of the liver-cells at the time of the atophan administration. Unger shows that there is a greater tendency to liver degeneration where there has been malnutrition and a decrease in the glycogen content of the liver cells. Then, as a result of this damage, intoxications will the more readily cause degeneration of the liver cells. Especially predisposed are alcoholics, pregnant women, and those who in the past have suffered from liver disease associated with jaundice. By what route the liver is attacked in the cases of hepatolysis is not quite settled. Whether the necrosis begins in the center or periphery of the acini is not believed to be of differential value. It may be by way of the general blood-stream, portal circulation, or ascending route of the biliary passages. Herxheimer[4] denies the latter possibility. In cases believed to be of intestinal origin, microscopic changes in the mesentery might be expected.

Due to any of the previously mentioned toxic factors, hepatitis (toxic jaundice) occurs. The amount of degeneration, or the amount of regeneration, will vary with the invididual case, thereby giving different pictures, depending on the balance between these two components. Therefore instead of talking of catarrhal jaundice it might be better to talk of hepatitis. Most mild cases result in healing without residual defect or interstitial cirrhosis. In those cases where there are greater degenerative manifestations with necrosis and dissolution of cells, it might be best to speak of hepatolysis instead of acute yellow

atrophy. If the hepatolysis or destructive process is quite extensive, we might then speak of liver atrophy. Herxheimer[4] makes the following classification: acute yellow atrophy for cases lasting less than three to four weeks, subacute yellow atrophy if the duration is up to seven or eight months, and chronic liver atrophy if the duration exceeds eight months. In the latter type there is noted a gradual change from a marked degenerative process to a wide-spread reparatory regenerative new-tissue formation, causing the development of new bile passages, liver-cell trabecles, and adenoma nodules. In other words, the hepatolysis frequently heals with the development of a hepatic cirrhosis of a large nodule type, which is pathologically distinguishable from the usual nodular Lænnec cirrhosis of the liver. These latter cases of regeneration may be wrongly diagnosed as tumors of the liver. Clinically, these cases of cirrhosis of the liver with adenoma formation (chronic atrophy) may be very difficult of differentiation from the usual cirrhosis of the liver and syphilitic cirrhosis. We, therefore, see gradual gradations from catarrhal jaundice—which according to Eppinger[5] is usually a mild hepatitis—to acute and subacute yellow atrophy of the liver, to chronic liver atrophy with resulting cirrhosis of the liver and nodular hyperplasia.

On gross appearance acute severe cases present marked yellow atrophy. The longer the duration, the more red there is mixed with the yellow, attended microscopically by necrosis, interstitial hepatitis, and increased formation of bile capillaries. In the more chronic cases, ascites and contraction with cirrhotic changes are noted. The liver process is not the entire picture, but only part and parcel of a toxic degeneration involving many organs. Febrile splenomegaly, red bone-marrow showing regeneration to compensate for extensive destruction of blood, fat necrosis of the pancreas, fatty degeneration of the heart and kidneys, and, in some cases, thyroid atrophy, have all been noted. As a rule, hemorrhagic gastro-enteritis, or hemorrhages into the mucous membranes and serous surfaces may be found. In the terminal stage there can usually also be found a hypostatic pneumonia.

As a rule, the cases start out with pains in the right upper abdomen or right back with vomiting. After feeling ill, tired, and weak for a few days to a week or two, jaundice usually follows. Severe vomiting, even of bilious character, may be present from the onset. Severe disturbance of the psyche, with sleepiness, stupor going on to delirium, are very important for the diagnosis of hepatolysis. Convulsions or twitchings in the presence of any jaundice, especially if associated with decrease in the size of the liver, is of great importance in the diagnosis or prognosis. The liver may at the very onset be enlarged. It usually soon begins to decrease in size so that it cannot any longer be felt under the rib margin. In the percussion of the liver, it is particularly important to measure out the left lobe of the liver by the Grocco method. As a rule, it is found that the left lobe of the liver suffers more, and decreases in size more rapidly. In one case, Herman Schlesinger observed that at the height of the disease the liver felt like a soft, plastic mass into which the finger could be pressed. Later the liver became harder and tougher, and finally the patient survived with the development of a coarse, nodular cirrhosis of the liver. The occurrence of a hemorrhagic state may set in after the jaundice, and be denoted by nosebleeds and purpura of the skin. The jaundice is, as a rule, very rapid in its development, varies greatly in its intensity, and may assume that of icterus gravis. Later on when the jaundice becomes very deep, it may assume a mahogany-brown color and give us an erroneous impression of a less intense degree, but a check-up by bilirubin estimations of the blood will show this to be erroneous. The spleen, while anatomically enlarged, is only occasionally to be felt.

The amount of urine decreases. It is usually dark brown, and contains traces of albumin, but no sugar. Hyaline and granular casts, red blood-cells, and bilirubin crystals may be found. Leucin and tyrosin are not as frequently found as one might be led to believe, as a rule, only occurring in those cases were there was a very acute intense hepatolysis. Leucin and tyrosin crystals even if present are not diagnostic. Leucin crystals may be differentiated from ammonium urate crystals

by the presence of prickles, the contents being lighter and showing no refractibility. The tyrosin crystals must be distinguished from bilirubin crystals, which are easily recognized by their intense red-brown color. Urobilin and urobilinogen, while usually absent, occasionally occur. Bilirubin is present, but decreased toward the end. The total nitrogen of the urine is increased. The excretion of ammonia and uric acid increases.

The duodenal contents may or may not show bile. As a rule, however, no bile acids are reported present.

As a rule, constipation occurs. The feces may be acholic and show bile at other times. The presence of bile or dark-colored stools speaks against common bile-duct obstruction of any cause whatsoever. The stools may or may not show red blood-cells or blood. In the presence of a marked hemorrhagic diathesis vomiting of large amounts of blood or blood in the stools may be present. This is particularly apt to occur if a chronic peptic ulcer is present.

The blood shows a markedly increased bilirubin. There are high aminonitrogen figures. The urea nitrogen of blood may be below 50 mg. per 100 c.c. The blood-sugar is increased and later decreased. The sugar tolerance is later decreased. Cholesterolemia is increased. Blood coagulation is decreased, and the bleeding time is increased early. The red blood-cells are usually increased, and the hemoglobin is increased. The red blood-cells may later on be markedly decreased. The total white blood-cells and polynuclears are usually increased. Leukopenia with relative lymphocytosis may occur.

The temperature varies. It may be normal or slightly increased. As a rule, a high rise of temperature occurs just before death.

It is important to obtain the typical odor of the breath due to the exhalation of amino-acids in these cases. The more intense the odor the worse the prognosis. Edema around the ankles may be observed and, after the sixth week in cases of subacute yellow atrophy, ascites and colics suggesting gall-bladder disease are not at all infrequent. This may lead to a revision of the diagnosis and an unnecessary operation. It is important to

avoid operation because the shock of even exploratory laparotomy in these cases may be more than the patient can stand.

The duration of the disease varies then, as a rule, with the severity of the process. It is important to remember that certain cases of chronic liver atrophy may all of a sudden present pictures of acute yellow atrophy, leading to exodus with sudden fever, sudden coma, hemorrhages, and increase of jaundice and ascites over that already present.

It is best not to give atophan or its derivatives in the presence of kidney or liver insufficiency. One might suspect liver dysfunction and a glycogen-poor liver where the blood-sugar estimation is below 100 mg. per 100 c.c. In such cases it would be best to give large doses of glucose, say 50 gm. by mouth, before the oral or intravenous administration in order to restore the glycogen content of the liver and so protect the latter against toxic influences. It should certainly not be used in the presence of so-called catarrhal jaundice. Before starting an atophan cure or giving an intravenous injection of an atophan derivative it would, therefore, be best to begin with small test doses, due to the fact that one cannot always predict a liver predisposed to toxic damage. One should certainly avoid the use of diiodatophan for cholecystography and use the much less toxic tetraiodophenolphthalein. About just as good results are obtained from moderate doses of atophan a few days each week as from long continuous usage. It is best to be given with large doses of sodium bicarbonate very well diluted, although cases in the literature are cited where, even in spite of this, toxic action on the liver has occurred. On the first sign of toxicity stop the use of the drug. If urticaria results, give calcium lactate; if gastro-intestinal or kidney symptoms, give glucose by mouth or in the form of a Murphy drip or, where the symptoms are at all severe, intravenously. In all cases where glucose is given, use insulin by hypodermic, in order to better fix the glycogen of the liver, and so protect it against further damage and aid in its recuperation.

The writer wishes to cite those cases of atophan poisoning of the liver obtained by gleaning the literature; then to cite 2 cases

of his own which he believes to be more than a mere coincidence, and which, fortunately, ended in recovery. He wishes thereby to call the attention of the medical profession to a further cause of toxic hepatitis and hepatolysis which must be considered in all obscure cases. In view of the fact, that at autopsy or operation the liver is practically the same as that of other causes of hepatitis or hepatolysis, it is important that inquiry as to the previous giving of atophan be made in all cases of suspected hepatitis or hepatolysis.

W. H. Willcox[3] reported having seen 3 cases of toxic jaundice after oral administration of atophan. One case proved fatal, that of a man of sixty-nine (in feeble health, and suffering from gout) who took 5 gr. of atophan with large doses of sodium bicarbonate in water three times daily for one week. Deep jaundice occurred in a few days. Signs of icterus gravis ensued, and death occurred in twenty-eight days. The stools were pigmented throughout, showing that there was no obstructive jaundice.

C. Worster-Drought[6] cites the case of a man of fifty-nine, suffering from recurrent arthritis, who took $7\frac{1}{2}$ gr. tablets of atophan three times daily for twelve days. He developed urticaria, and stopped the atophan for three weeks. He then took one $7\frac{1}{2}$-gr. tablet to be followed the next day by pruritus and urticaria. Ten days later moderate jaundice, without enlargement of the liver or tenderness, appeared. This regressed after several weeks. It is highly probable that prompt omission of the drug was responsible for the saving of the patient's life.

G. Evans[8] reported 3 cases of severe poisoning with jaundice, 1 with repeated vomiting, following oral use of atophan, even though given with large doses of sodium bicarbonate. One patient developed symptoms on two separate occasions.

C. J. L. Wells[9] observed a woman, sixty-three years old, giving a negative gastric history, but suffering rheumatoid arthritis for years. She took $7\frac{1}{2}$ gr. atophan tablets three times daily for five months. At the end of three months she began to vomit, which increased to the time of her death. One week before death she complained of pain over the liver area. Liver tenderness,

rapid pulse, absence of fever, and slight albuminuria were noted. Three days later jaundice developed which was followed in two days by stupor, coma, and death. At the postmortem examination, a very small, shrunken liver which histologically presented the picture of acute yellow atrophy with complete absence of normal liver tissue was found. No gall-stones were found either in the gall-bladder or bile-ducts to explain her jaundice.

L. G. Glover[10] published the case of a woman who went to Germany for treatment for rheumatism. There she received five intravenous injections of atophanyl, 5 c.c. each, at intervals of one to two days. Upon her return to England, she received five more injections of 2 to $4\frac{1}{2}$ c.c. each, at intervals of four days. After the last injection she developed indigestion, and in five days jaundice appeared. She made a recovery. The subsequent details are not given.

D. Klinkert[11] reports a female patient suffering from subacute articular rheumatism, who, after receiving fifteen injections of atophanyl followed by oral use of 1 tablet of atophan three times daily for one month, developed gastro-intestinal disturbance and jaundice, enlarged liver, bile in urine, no splenomegaly, no fever.

G. W. Rake,[12] in an article entitled "Subacute Yellow Atrophy After Atophan," relates the history and autopsy findings of a patient aged fifty-four, alcoholic and gouty, who took an excessive amount of atophan for relief of gouty pains. Sharp epigastric pains and vomiting occurred with slight jaundice, which in two days became a deep persistent mahogany-color. Recurrences of severe colics and vomiting ensued. The urine became dark brown. One month after the onset, the liver could be felt one fingerbreadth below the right costal margin, and was very tender. The Wassermann reaction was negative. A diagnosis of gall-stones was made, but operation failed to find gall-stones, and the liver was small and irregularly nodular. Two days after operation drowsiness set in, and the patient died the next day. At the postmortem examination, the liver was small and weighed only 1150 gm., its greatest decrease being that of the left lobe. The capsule was wrinkled and thickened. Irregular green

nodules of regenerating liver-tissue were noted. On cut surface, irregular central areas of red tissue were seen chiefly around the central veins, with areas of degenerative change toward the surface. Microscopy revealed slight periportal fibrosis and small cell infiltration. The stroma was slightly congested, and some of the liver-cells showed fatty degeneration. The small ducts contained bile-pigment, but there was no increased growth of the biliary system. The liver-tissue was almost entirely destroyed, with the exception of the bile-ducts. Areas of congestion and hemorrhage, signs of beginning organization with small cell infiltration and isolated strands of fibroblasts were noted. The kidneys showed cloudy swelling with fatty degeneration of the convoluted tubules, and some thrombosis of renal venules. The suprarenals showed some capsular congestion and hemorrhage.

H. Hitzenberger[13] cites the case of a twenty-one-year-old woman suffering from diabetes insipidus and occasional febrile attacks. On the day of admission she became afebrile. A slight tenderness under the right ribs suggested a possibility of gall-bladder disease, and cholecystography with diiodatophan (Biloptin) was made. That same night severe distress and vomiting, the next day slight jaundice, and on the third day fever with steadily increasing jaundice occurred. The patient vomited everything and became confused, stuporous with occasional convulsive seizures. The patient died on the tenth day with a typical picture of icterus gravis, which led to the clinical diagnosis of acute yellow atrophy. On the eighth day of the disease a generalized erythematous urticarial rash had appeared. Very high bilirubinemia had been present. At postmortem examination, the diabetes insipidus was explained by a walnut-sized tumor of the pituitary stalk. The gall-bladder mucosa was delicate, the hepatic and common bile-ducts showed no obliteration and contained a slight amount of mucoid bile, the spleen was somewhat enlarged, and its pulp was soft. The liver projected two fingerbreadths below the free border of the right ribs. The lower border was rounded, the capsule smooth, the consistency somewhat diminished. On cut surface the paren-

chyma appeared dark red, with a grayish admixture. The centers of the acini were brown, while the periphery of the acini were narrow and of grayish-yellow color. On histologic examination of the liver, there was necrosis here and there in the centers of the acini; in many areas round-cell infiltration with beginning necrosis of the surrounding liver-cells; in the periphery of the acini, a narrow fat-infiltrated zone. These are all evidences of severe damage of the liver, though not the picture of the fully developed, acute yellow atrophy but certainly the beginning of such a state and might, therefore, be termed acute hepatitis with beginning hepatolysis.

He reported a second case of a powerful male of sixty, with a tumor in the right hypochondrium thought to be gall-bladder. After giving diiodatophan (Biloptin) for cholecystography, jaundice appeared the next day, he felt sick, vomited, had a bad taste, anorexia, and severe pruritus with marked bilirubinemia. The jaundice and the general symptoms gradually disappeared in ten days with attendant desquamation of the skin. At a subsequent operation no change in the bile passages was present.

G. Schwartz[14] the next week before the same society reported a case of toxic jaundice occurring after the use of diiodatophan for cholecystography, though he had splendid results in 24 other cases. The technic was the usual one, 5 gm. having been given by mouth. The *x*-ray findings the next day showed a normal, well formed gall-bladder. At that time the patient complained of mild gastric distress, but did not appear seriously ill. The day after, distress persisted. On the third day, mild jaundice with persistent nausea and vomiting set in. On the fourth day, the jaundice became very marked, and the day following her condition became very serious. Food could not be taken because of the persistent nausea, which was finally controlled by rectal suppositories of morphin and atropin. Glucose infusions with simultaneous insulin injections were then given.

The above case was reported on the twelfth day of the patient's illness. The temperature was then normal, there was no jaundice, there was good heart action, but her condition was still critical. He believed that this particular patient presented

an oversensitivity of the liver, and that the patient belonged to the group who are sensitive to salvarsan, reacting to it with jaundice; or to those cases of lues, developing luetic hepatitis; or to those cases of pregnancy which react with hyperemesis and acute yellow atrophy of the liver. The report of this case was followed by lively discussion, in which Singer and Haudek participated, reporting additional cases.

S. Singer[15] stimulated by Hitzenberger's report, a week later reported a case of a fifty-six-year-old woman, suffering from recurrent pains in the right upper abdomen, and vomiting. On the day of admission to the hospital she had high fever. After that she was persistently afebrile. On examination in a warm bath, a 2 cm. long, hard tumor, showing slight respiratory mobility, could be felt two fingerbreadths below, and somewhat to the right of the umbilicus. It was interpreted as gall-bladder. The urine showed red blood-cells, persistently, with albuminuria. On intake of 40 gm. of galactose, 0.61 gm. were excreted. The bilirubinemia was 0.52 mg. per 100 c.c. Suspecting a gall-bladder tumor, diiodatophan (Biloptin) was given for cholecystographic purposes. A few hours later the patient began vomiting, which became incessant the next day, and lasted for two weeks in spite of all therapy. Definite jaundice appeared on the day after the diiodatophan was given. The bilirubin of the blood-serum increased. The patient received 10 c.c. of 40 per cent. dextrose and 5 units of insulin twice daily, with moderate decrease of the bilirubinemia. On the fourteenth day aspiration bronchopneumonia, with exodus two days later. The autopsy findings were that of a recurrent, subacute, bacterial endocarditis of the mitral valve, hemorrhagic nephritis, gall-stones in the gall-bladder, with adhesions of the gall-bladder to the omentum. Microscopic examination of the liver showed small round-cell infiltration of numerous areas. While the diiodatophan was not the direct cause of death, the jaundice and the uncontrollable vomiting due to the toxic hepatitis were certainly due to it. No evidences of bile-duct obstruction were present.

M. Haudek[16] in discussing G. Schwartz's case reported that of a thirty-year-old physician who, following the diagnostic use

of diiodatophan (Biloptin), developed severe nausea, vomiting, and jaundice which had in the main regressed at the time mentioned.

O. Kingreen[17] reports the case of a woman of thirty-one, suffering with gall-stones for two years, who, following the use of diiodatophan for cholecystography, was operated upon the next day under ether anesthesia. The gall-bladder was found markedly dilated and slightly inflamed, surrounded by numerous adhesions which constricted the cystic duct. The common bile-duct was negative and no stones were present in the hepatic and common bile-ducts. Cholecystectomy was performed. The gall-bladder wall was thickened, its mucous membrane swollen, and numerous stones, together with thickened bile, were present. Two days postoperative: moderate fever, beginning jaundice, no pains, bilious vomiting. The next day the jaundice increased, pulse small and slow, abdomen soft, no pains. The jaundice rapidly and steadily progressed, restlessness appeared, the urine showed slight albumin, casts, and red blood-cells; stools contained bile. After four days of severe illness, the general condition improved and jaundice gradually regressed. One month later the patient still looked badly, the mucous membranes were very pale, and a very slight icterus was still present. Opposed to the diagnosis of common-duct stone was the absence of pain, and normal-colored stool. In view of the excellent technic, there was no reason to assume damage to the liver or to the common bile-duct. He also believed the jaundice could not be explained by an excess of bile formation, but rather due to severe damage of the liver.

Case I.—J. P., physician, age thirty-three, came into my office July 8, 1927, with a complaint that four weeks ago jaundice had appeared. Five months previously he had an infected tooth pulled which was followed by fever, chills, toxic arthritis, and backache. On questioning he stated that for the relief of the pain he began the irregular use of atophan five months ago, taking about 100 gr. in all during a period of three months up to the onset of the present illness. This began five weeks ago with nausea which, together

with weakness, loss of appetite, and distressing heartburn has persisted. Four weeks ago jaundice came on suddenly with marked itch. There was no pain or fever. There has been a loss of 15 pounds in the past week. The jaundice persisted and increased. He stated that the urine showed bile at all times, faint trace of albumin, a few casts and epithelial cells, and that the stools had persisted clay-colored. The vomitus had never been greenish. No hemorrhages had appeared. Examination showed a deep mahogany-brown jaundice. The liver was not palpable and its edge percussed above the ribs, the left lobe of the liver was small by the Grocco method of percussion. The knee-jerks and pupillary reflexes were normal. There was no evidence of fluid on percussion of the flanks, no dilatation of the veins of the abdomen. The spleen did not percuss enlarged. On inflation of the colon no enlargement of the spleen, while the liver appeared smaller than normal could be seen by fluoroscopy. The heart, lungs, and diaphragm were normal. He was advised to enter the hospital, which he did on July 19th. At that time the liver was definitely palpable one fingerbreadth below the costal margin. The spleen was not palpable. The patient stated that he felt somewhat better. He had in the meantime been advised to be on a high carbohydrate diet. There was no fever or increase of pulse rate, nor any abdominal pains or colic. Thorough laboratory investigations were made with the following more important data. The blood Wassermann was negative. The blood-bilirubin on the 20th was 38 units; on the 23d, 20 units; on the 27th, 19 units, and on the 30th, 3 units. The icteric index on the 16th was 75; on the 20th, 60; on the 24th, 75; on the 28th, 75; and on the 30th, 48. The urine on the 17th showed urobilinogen absent, urobilin 500 dilution units, tyrosin present. On July 17th, 20th, and 21st, marked bilirubin was present in the urine; on the 28th it was found decreasing, and on August 1st only a very faint trace was present. The feces showed bile on the 18th and 20th. Blood-study showed hemoglobin, 70 per cent.; platelets, 250,000; leukocytes, 12,600; red blood-cells, 5,120,000. The bleeding time was one and a half minutes; color index, 0.68; coagulation time, seven minutes; polynuclears,

72 per cent.; eosinophiles, 3 per cent.; small lymphocytes, 20 per cent.; mononuclears, 5 per cent. Anisocytosis was slight; reticulation, 0.8 per cent. Hemolysis began at 0.44 per cent. saline, and was complete at 0.30 per cent saline. Two weeks later the blood-count was 3,500,000 red blood-cells; hemoglobin, 85 per cent.; 8000 white blood-cells; 60 per cent. polynuclears, 3 per cent. mononuclears, and 37 per cent. lymphocytes. The treatment had consisted of a high carbohydrate diet, with 5 units of insulin, hypodermically, three times a day. On discharge, August 2d, the size of the liver was about normal. There was no enlargement of the spleen and no ascites.

October 15th he was re-examined and the liver edge was just palpable and firm. No spleen was palpable. The urine showed no bile, the feces were of normal color.. He stated that he felt slightly weak and had some pain in the right back.

This case in all likelihood presents the toxic action of atophan on the liver, with resulting severe hepatitis and slight hepatolysis, followed by active liver regeneration. Whether any cirrhotic changes have occurred, time alone will tell. In the meantime careful observation is indicated, and a high carbohydrate diet is advisable to render the liver less vulnerable to future additional toxic damage.

Case II.—B. Z., married, age thirty-nine, consulted me on July 29, 1927. About four months ago he caught a "cold in the back." Lately he had taken twenty-five $7\frac{1}{2}$-gr. atophan tablets. He developed nausea, followed in three days by jaundice which has continued. He had no pain. The stools were colorless. He felt weak, tired, there was no itching, no fever. His appetite was very poor, bowels fair, slept well and lost considerable weight. Marked jaundice was present. By Grocco the left lobe of the liver was smaller than normal. His pulse was 60. The urine showed specific gravity of 1018; indican, 2 plus; urobilinogen, 2 plus. He was admitted to the hospital on July 29, 1927. His temperature on admission was 98.4° F.; pulse, 84; respiration, 22. He presented evidence of deep jaundice, clay-colored stools, bile in the urine, and bilirubinemia. On a

high carbohydrate, low protein diet with insulin his condition improved markedly, the bilirubin in the blood coming down from 13 to 2.5. The important laboratory findings while in the hospital were as follows: Blood Wassermann was negative. Icteric index, July 29th, 80; August 3d, 58; August 9th, 32. A complete blood-study made on July 29th showed red blood-cells, 5,040,000; hemoglobin, 87 per cent.; color index, 0.87; platelets, 200,000; leukocytes, 10,000; polynuclears, 60 per cent.; eosinophiles, 1 per cent.; small lymphocytes, 31 per cent.; mononuclears, 8 per cent.; bleeding time, three minutes. Urinalysis on July 30th gave a specific gravity of 1010, alkaline reaction, bile, 4 plus. Gastric analysis on July 30th, showed free hydrochloric acid 10, combined acidity 35, total acidity 45. He was discharged from the hospital on August 17th, markedly improved.

He stayed home one week, felt quite well until he went to work, after which he had some pain in the right upper quadrant, right axilla, right back, and right buttock. His appetite was good; his bowels were good. On re-examination September 1st, his weight was $169\frac{1}{2}$ pounds, his blood-pressure 116/76, urine urobilinogen was 2 plus, indican, 2 plus. His backache was better. He had moderate weakness, but his jaundice had disappeared. He had local pains in the right sacro-iliac joint. The spleen percussed enlarged. The liver and spleen were not felt. Fluoroscopy with colon inflation showed spleen apparently enlarged with the liver probably diminished in size in the antero-posterior diameter, being displaced anteriorly by the distended hepatic flexure of the colon.

In this case, we are probably dealing with toxic hepatitis and slight hepatolysis due to atophan, with some secondary reparative cirrhotic changes.

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INTERPRETATION OF EYE PATHOLOGY. CLINICAL PERIMETRY—ITS VALUE TO THE INTERNIST

THE visual-field studies have so often been looked upon as a refinement of ophthalmologic technic, that any practical application seems far removed from the field of the internist. In fact, many feel that it still belongs in the physiologic laboratory as a curiosity and novelty. Such a view means that the tremendous growth in this branch has been overlooked. To neglect it entirely as a diagnostic aid is to admit a lack of progress during the past twenty-five years. It is, therefore, proposed to point out certain clinical relations in the hope that more interest will be aroused.

The ophthalmologist who depends solely on either a test of visual acuity or the ophthalmoscope to disclose pathologic changes, would be like the internist who depends upon the pulse rate and volume for all his information on the cardiovascular system. Visual-field studies are at present the most reliable and helpful means that we have of making an accurate and permanent record of functional and organic damage to the optic mechanism, and so indirectly of its derangements through other structures.

A **definition** is seldom a lucid means of introducing an unfamiliar subject, but perhaps an analogy is permissible.

Suppose a patient presented himself with a severe lower thoracic pain. Such a location, and a vague description of its character might be the only available evidence of a lesion. Suppose that this manifestation could be so magnified and visualized as to permit its complex features to be separated for analysis. Suppose that by this means not only the nerve which was exciting the response could be identified, but that the

actual fiber bundle could be determined and the point in its course located. With the data derived, quite conclusive evidence

Fig. 167.—A lead model (exact measurements) of the optic pathways was placed in a skull. This plate visualizes the vital relations which the pathways have to the intracranial structures. Particularly interesting in this picture are the relations of the nasal accessory sinuses to the optic nerves: 1, Left eye; 2, left optic nerve; 3, optic chiasm; 4, left optic tract; 5, optic thalamus; 6, optic radiations; 7, mesial aspect, posterior pole, occipital lobe (cortical center of vision). It will be noted that that portion of the optic pathways on the right side, is missing from the optic tracts (8) back. This was left out so as to make localization less confusing. The reader should visualize the missing structures for the opposite half.

might be amassed which would show the relation of such a lesion to adjacent organs. Furthermore, such information might easily

unfold etiologic factors which, when taken with other or later findings, would clinch a diagnosis. To be sure, these conditions have been simulated in efforts to map areas of reduced or increased skin sensitivity, but present methods are not only comparatively crude and unreliable, but opportunities for the application of such testing are relatively rare.

Anatomic Relations of the Pathways.—With these ideal conditions in mind, consider for a moment the wonderful aid to diagnosis which the visual fields offer (Fig. 167). In the first place, we must realize that in the optic pathways we have an extremely responsive system passing through the brain—in direct relation with the ventricular and subarachnoid fluids, and exposed to changes of the vascular and lymphatic systems. Variations in the conductivity of the optic pathways are not only demonstrable, but they are capable of projection upon a curved or flat surface in such a way as to result in tremendous magnification.

Clinical Standards.—Tests with the perimeter and tangent screen have been refined to such a degree in the past few years that certain *definite standards may be accepted.* In order to do this, however, we have to discard all features which are unsettled or in dispute. From a careful review of the literature, and from conclusions drawn from special investigations to this end, the following may be laid down as a temporary plan to adopt.

1. Color fields must be discarded as at present they are incapable of standardization.

2. Artificial (daylight) standardizable illumination alone must be used.

3. The principle of "quantitative perimetry"* should be adopted (white objects).

* The writer does not approve of the expression "quantitative perimetry." This implies that the method determines the boundaries of zones of visual acuity. Such cannot be the case because a single object is used. To lay down visual acuity isopters it would be necessary to outline the acuity fields by using an object composed of two dots separated by an interval equal to half their combined diameters. The term has, however, been used so frequently as to have gained general use.

4. The use of modern instruments which permit the conditions of testing to be reproduced for all types of cases and under all conditions should be encouraged (ambulatory and non-ambulatory).

Such statements will, of course, meet antagonism, because surgeons, internists, and neurologists have for years been called upon by ill-founded tradition to ask for certain types of tests irrespective of their accuracy and actual value.

Color-fields.—Perhaps those who have been in the habit of using color-fields will be most incensed at this condemnation.

It is, therefore, necessary that we state at some length the grounds on which the objection to color-field evidence is based. In order even to establish the limits of the normal color-fields it is necessary to test the subjects very thoroughly for any form of *congenital color-blindness*. Many of us do not come up to standard in this respect, as can readily be shown by running through the plates of the Stilling[1] test. In these perimetric studies we ask our patient not only to make very definite discriminations of color, but also to judge carefully the tints and shades, because these determine the relative color defects. The most vital changes to disclose are always the border-line ones, because such slight defects not only show the site of the condition, but also allow one to determine the stage, rate of progress, and likely complications. If we are satisfied that we have a patient *psychically satisfactory* for color studies, it is not enough to map with one color, but *three or four colors* must be used and, moreover, *three or four sizes* of each color. All this having been done, our results may be entirely unsatisfactory because the test has been prolonged and the mechanism has become so *fatigued* as to give unsatisfactory results. Frequently, *lighting conditions have changed* during this protracted ordeal. It has been repeatedly shown, that all visual-field work is influenced by changes in the intensity of light. Variations in the intensity of light on the perimeter and campimeter can make the color-fields vary greatly. It is seldom possible to establish sufficiently ideal or standard illumination for color-fields except, perhaps, in a few patients able to go to the ophthalmologist's office. In

order to justify the use of colors, some workers try to wait for ideal natural light. This certainly is not practical, even in chronic cases, particularly when we realize that the mean of monthly sunlight readings may be anywhere from *2200 candles per square foot to 270 candles per square foot* (June and December). That, at the same time of day, it may be from 500 to 5 candles per square foot, as a mean monthly reading.[2] We must, therefore, *not attempt to use daylight*, particularly if we work with colors, and if we hope to arrive at usable standards.

The writer feels he can safely say that if colored objects had never been used that branch of ophthalmology having to do with visual-field study would have progressed just as rapidly. On the other hand, much energy used in that endeavor might have advanced the study much further by the use of white objects. We do not mean to say, however, that color-studies have no place in ophthalmology, but we do wish to emphasize the point that the work so far done is so unsettled and so incomplete as to make the clinical application of the color-field studies decidedly unreliable, if not unsafe, for internal medicine to interpret.

*No field defect appears for colors alone. If it is not demonstrable with white objects, it is only because the technic used was faulty.**

It is not difficult to *standardize artificial light* so as to come well within the allowable limits of error for *small, white objects*. This is practical even in bed-patients by the use of modern instruments and technic. If we review the conclusions of those workers who have contributed to the growth of the visual-field study, be it through the surgical branch as that of Cushing and Walker,[3] Uhthoff,[4] etc., or through the medical branch as that of Peter,[5] Lloyd,[6] Traquair,[7] Igersheimer,[8] etc., we are impressed over and over again with their emphasis of the use of small, white objects of various sizes to map the fields. Some

* The writer does advocate a red glass[13] before the patient's eye at times when using a white object, but this is not the same as mapping with a red object—it has the effect of simply reducing the illumination, and probably has nothing to do with the problems of color vision in the finer sense.

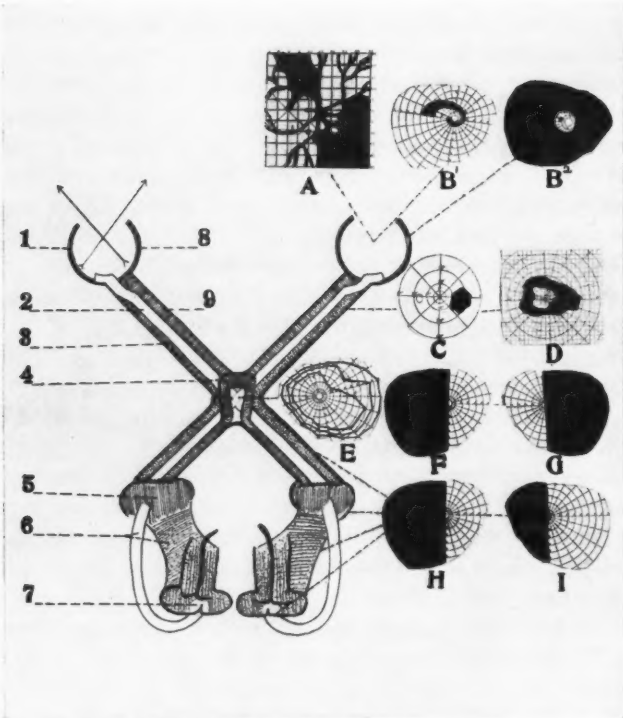

Fig. 168.—This is a very diagrammatic representation of the optic pathway and a few ideal fields seen with lesions at the sites indicated. 1, Temporal retina; 2, papillo-macular bundle of nerve-fibers; a lesion of which produces a central scotoma—loss of reading vision; 3, uncrossed fiber-bundles from the left temporal retina—damage to these shows a defect in the nasal field, as indicated by the large arrow (left eye); 4, the optic chiasm showing the semidecussation of the fiber bundles; 5, the external geniculate body; 6, the optic radiations; 7, the location of the cortical visual center and particularly that of the macular bundle (no attempt is made to show that these fibers also undergo a semidecussation).

The charts are also very diagrammatic: *A*, Plotted by following out the blood-vessel shadows (angioscotometry). This represents a composite of numerous angiopathic lesions; B^1, two simple fiber-bundle defects, such as are most typically seen in glaucoma and early pressure on the optic nerve; B^2, a concentric contraction when the pressure may have involved all the peripherally placed bundles in the nerve—seen in numerous diseases; *C*, an enlarged blind spot seen most typically in certain cases of increased intra-

of them do refer to the use of colors, but in such a half-hearted way as to imply that they do so only out of deference to tradition.

Modern Material on Interpretation.—There are *no complicated rules to remember in the interpretation* of visual-field maps, but we must have a clear mental picture of the *anatomic relations* of the optic pathway, not only grossly but also of the arrangement of its fiber bundles. The work of Henschen[9] is generally accepted as it has been elucidated and corroborated by many workers. The newer books on perimetry, notably those of Lloyd,[6] Peter,[5] and Traquair,[7] review it satisfactorily. These works also summarize the duplicity theory of the retinal functions in a very attractive way. This theory helps to explain many of the characteristics found.

It is not expected that the internist be in a position to explain every visual-field defect by keeping at his finger-tips the mechanism of every possible process which may give rise to a disturbance of the functioning of the visual pathways, but he certainly should know how and where to look up the modern reliable material for a special case, and should be expected to discuss the findings intelligently with the consulting ophthalmologist. To this end he should refer to the two recent contributions in French; the one by Schiff-Wertheimer[10] (Fig. 168, *A* and *I*), who elucidates the syndromes of homonomous hemianopsia occurring with the various vascular lesions of the brain associated with softening, and the other by Favory[11] (Fig. 168, *E*, *F*, and *G*), on the syndromes of the optic chiasm.

It is necessary to recall that the lesion can have its origin in the eye itself, so that the defects in the fiber bundles may

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cranial pressure and nasal accessory sinus disease; *D*, a ring scotoma seen in a wide variety of cases; *E*, this shows the "*Isopters*" of fields as mapped by the method of "quantitative perimetry," the field plotted with the largest object being outermost, the smallest innermost. Note that the smaller objects bring out the sector or *quadrant defect* in the upper temporal field. As the case advances the lower temporal quadrant is lost, thus there results a temporal hemiloss. This same change occurring in the two eyes gives the maps as seen in *F* and *G*; *F*, *G*, bitemporal hemianopsia; *H*, *I*, homonomous hemianopsia. This is found with lesions behind the chiasm. The particular location is settled by the character of those fields, pupillary signs, and the other manifestations from adjacent structures.

start in the retina. Igersheimer[8] has worked out this system (Fig. 168, *B*). Also those defects of the retina having their origin in the angiopathic processes have been elucidated by Evans[12, 13] (Fig. 168, *A*). Localized sources must not be confused with changes having their origin more centrally, yet their interpretation is often very directly helpful to the internist.

Types of Defects for Interpretation.—The visual field may show depression over its entire surface or an irregular defect, usually at its border. When a number of plottings are made with small white objects of decreasing size, the larger forms the outer zone, the smaller the more inner zones. If the depression is uniformly of the entire field, the different objects will form zones of progressively smaller limits and they will be spaced evenly. If, on the other hand, a certain bundle of nerve-fibers is beginning to show a depressed function, a finger-like erosion may be evidenced in the field as mapped with the more minute objects, and perhaps not be apparent with the larger (Fig. 168, *E*). We can state from such a case that unless we are able to arrest the progress of the lesion, we can expect a large defect of the visual field to develop for the larger objects. In this way "quantitative perimetry" supplies not only a means of earlier localization, but also a means of following the course. As a lesion clears up, the smaller object-fields improve first. These changes are particularly well illustrated in simple pressure cases—pituitary disease.

Instruments and Charts.—A number of perimeters and tangent screens (the smaller ones are sometimes called campimeters and scotometers) are in general use. Any variation in size or range of these necessitates a slightly different form of chart. Most are printed as concentric circles with radiating spokes from the central point. Some of the tangent screen charts are printed as rectangles, because a tangent screen represents a perimeter flattened out. With very rare exceptions, all charts are marked out in lines corresponding to degrees or multiples of degrees so that, if studied, they will be clearly comprehended.*

* The illustrations accompanying this paper are purposely reproduced from various types of the more commonly used charts. The plottings are very diagrammatic so as to emphasize the points in the text.

Application to General Problems.—To illustrate the breadth of application of visual-field disturbances, the following outline summary of the above-mentioned workers, while necessarily very incomplete, will serve to demonstrate the relations of the studies to internal medicine.

A. Angiopathic ocular disease associated with visual-field defects (Evans) (Fig. 168, *A*).
   I. Angiosclerosis as:
      (*a*) Arteritis.
      (*b*) Phlebitis.
   II. Retinitis as:
      (*a*) Arteriosclerotic.
      (*b*) Renal.
   III. Certain toxic lesions as:
      (*a*) Quinin amblyopia.
      (*b*) Auto-intoxication.
   IV. Certain degenerative changes as:
      (*a*) Retinitis pigmentosa.
   V. Certain specific diseases as:
      (*a*) Tuberculosis.
      (*b*) Syphilis, etc.

B. Fiber-bundle defects, ocular and central (Igersheimer).
   I. Optic Atrophy (concentric contraction, Fig. 168, B^2).
      (*a*) Pressure on nerve.
      (*b*) Postinflammatory.
   II. Multiple sclerosis (ring scotoma, Fig. 168, *D*).
   III. Nasal sinus disease (enlarged blindspot of Fig. 168, *C*).
   IV. Chronic glaucoma (single bundle defects, Fig. 168, B^1), etc.

C. Visual fields associated with syndromes of the optic chiasm (The "pathognomonic" field of chiasm disease is the more-or-less regular symmetrical bitemporal hemianopsia). Favory works out the following (Fig. 168, *F* and *G*):
   I. Chiasm syndrome of tumors affecting the
      (*a*) Hypophysis.
      (*b*) Not of the hypophysis.

II. Chiasm syndrome of syphilis:
  (*a*) With neuritis.
  (*b*) With meningitis.
  (*c*) With infundibular involvement.
  (*d*) With vascular periostitis.
III. Chiasm syndrome of encephalitis.
IV. Chiasm syndrome of toxic origin, etc.

D. Visual fields associated with homonomous hemianopic syndromes in vascular cerebral softening. (The "pathognomonic" field of a lesion posterior to the optic chiasm is a more or less regular and symmetric—homonomous (same-sided); hemianopsia (half vision)—(Fig. 168, *H* and *I*). Schiff-Wertheimer works out the following:

I. Hemianopic syndrome with lesions of the posterior cerebral artery.
II. Hemianopic syndrome with lesions of the sylvian artery, as with:
  (*a*) Deep sylvian involvement.
  (*b*) Superficial sylvian involvement.
  (*c*) Total sylvian involvement.
III. Hemianopic syndrome with lesions of the anterior choroidal artery, etc.

Note.—It must not be understood that these authors are the only ones taking their respective viewpoints. They are selected because their material has been developed along lines of particular value to the internist.

Conclusion.—The writer feels the entire inadequateness of this paper in the sense of supplying, definitely, directly applicable material. Such has not been his endeavor. The subject has been so completely overlooked from the standpoint of internal medicine that this communication can be regarded as no more than an introductory remark. It is hoped that in the near future a more concrete material will have accrued, so that some plan may be mapped out which can be used as an outline from which the internist may proceed to analyze such evidence for diagnosis.

In the past we have had works on "Medical Ophthalmology."

The subject has grown so fast—for ophthalmology is always on the wave-front of medical progress—that in order for the material to be wieldy it must be split into its component parts. Both the surgeon and the physician have developed ophthalmology in England—each from his respective viewpoint. Ophthalmology in the United States seems to have much more in common with internal medicine than it does with general surgery. This relation is becoming more noticeable, and it is in this way that the value of clinical perimetry to the internist is becoming more and more obvious.

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DYSTROPHY IN ARTIFICIALLY FED INFANTS

CHRONIC nutritional disturbances are not as frequent as in former years because the art of feeding by well-balanced formulas, containing all the elements required, is better understood. Disturbances do occur, however, and when present require as much skill in the handling as is necessary for the surgeon to possess in the performance of the most delicate operation. It is no exaggeration to state that in chronic nutritional disturbances judicious and accurate treatment will save life, and that lack of appropriate treatment will result in disaster. Keeping our hands off and simply waiting for the healing power of nature to effect a cure, as we are compelled to do in so many diseases, will not suffice here.

For a better understanding of nutritional disturbances, it is necessary to present a systematic classification. Since the normal is always taken as a standard in evaluating any disease process, it is essential here, too, to familiarize oneself with a standard by which an infant is judged. Finkelstein, whose classification with some modifications will be employed, divides all infants into three groups: the eutrophic, the paratrophic, and the dystrophic. It is the last group with which we are mainly concerned. An infant is said to be in a state of eutrophy when it has a normal constitution, when it is making proper and satisfactory progress on a well-balanced dietetic regimen, when it is hydrostabile, and has a high degree of immunity. In the second group, paratrophy, are included infants in whom the outstanding symptom of dystrophy, namely, in-

adequate weight, is absent. Such infants may be of normal weight, slightly below normal weight, or even over-weight, but they present abnormal constitutional tendencies which have not been properly taken into consideration in the dietetic regimen. In this group belong the hypertonic, hypotonic, bloated, and adipose infants.

The third group consists of infants who are dystrophic. Two symptoms are characteristic of this group: first, the infants are always definitely below weight, and second, they have a lowered immunity to infections. Not only is the dystrophic infant more susceptible to infections, but its reaction to an infection is also quite different from that of a eutrophic infant. For example, an attack of nasopharyngitis in a normal infant subsides in a few days with no appreciable change in the general condition of the infant. In the dystrophic infant the infection lasts much longer, there is more likelihood of the development of a pulmonary complication, and the general condition of the infant suffers.

Dystrophy may be subdivided into two large groups, depending upon whether the infant is hydrolabile or hydrostabile. Dystrophy in a hydrostabile infant is termed "dystrophia simplex," or the simple form of dystrophy; it may or may not be accompanied by diarrhea. Dystrophy in a hydrolabile infant is termed "dystrophia hydrolabilis," and is practically always accompanied by diarrhea. In simple dystrophy the infants do not gain weight or lose weight gradually. In the second group the loss of weight is marked, rapid, and progressive. The severest form of dystrophia hydrolabilis is termed decomposition or atrophy, and it is characterized by extreme emaciation with an almost complete disappearance of subcutaneous fat. According to L. F. Meyer, the best criterion of an infant's general condition is obtained by close observation of the deposition of subcutaneous fat. In his clinic the subcutaneous fat deposits of the abdomen are measured regularly by means of a slide-rule, and the figures are noted on the chart. In dystrophy the disappearance of the subcutaneous fat is moderate and usually involves only the trunk and abdomen. In decomposition or

atrophy, the disappearance of subcutaneous fat is general and involves even the face.

It is necessary to digress at this point in order to define hydrolability and hydrostability. Growth occurs because of cell imbibition; protein, water, salts, and carbohydrates are equally concerned in this process. If one or more of these elements are missing, cell imbibition will not take place, and failure to gain in weight, or even loss of weight, will occur. The water is held at first in an unstable combination, but later becomes more firmly fixed by some mechanism with which we are not yet entirely familiar. It appears, however, that the lipoids are a factor in producing a more stable combination of water in the cell. The ability of the cell to retain water under various conditions, *e. g.*, infections or withdrawal of food, will depend upon the type of water fixation present. Infants differ in their ability to retain water in the tissues. When water is readily given up, *i. e.*, when water instability exists, the infant is termed hydrolabile. Water instability may be present at birth or it may be acquired later. Infants born with water instability are candidates for decomposition from birth. Hydrolability may be acquired when severe injury to the tissues occurs, as in long-protracted inanition. Other infants, in whose tissues the water is fixed in a stable combination, tenaciously retain the water and are not so readily predisposed to decomposition. Thus, when salts and carbohydrates are withdrawn from the diet of a hydrostabile infant, there is, as a rule, an initial loss of weight of 50 to 100 gm., after which no further loss occurs. The hydrolabile infant under similar conditions, however, loses weight very rapidly; the loss is continuous, and may amount to 250 to 500 gm. in twenty-four hours. Death may even result unless the missing components in the diet are supplied.

As a rule, little difficulty is encountered in determining whether an infant belongs to the eutrophic, dystrophic, or atrophic group. For intelligent treatment, however, the determination of the causative factor is essential.

Simple dystrophy may be divided into three large groups, based on etiology:

1. Dystrophy Due to Qualitative or Quantitative Inanition.—Qualitative inanition may be due to:

(*a*) Insufficient water—as when concentrated feedings are given.

(*b*) Insufficient carbohydrate in a mixture which contains sufficient milk to meet the caloric requirement of the infant (Milchnährschaden; milk injury). In Milchnährschaden there is at first a stationary weight in spite of the adequate caloric intake; later, loss of weight which may be large and rapid occurs. It was formerly believed that diminished absorption of fat and calcium was responsible for the loss of weight. It appears more logical, however, to explain the failure to gain as due to the absence of carbohydrate or the inadequate supply of carbohydrate in the diet, with the consequent removal or reduction of one of the factors which is essential for cell imbibition. In milk injury insoluble calcium soaps are formed in the intestine; as a result, the stools become hard, dry, and white, and roll off the diaper without staining it. The stools are white because bilirubin is reduced to hydrobilirubin in the presence of excessive putrefaction.

(*c*) Insufficient milk in a mixture which consists almost exclusively of carbohydrate (Mehlnährschaden, starch injury). Mehlnährschaden is produced when cereal or flour mixtures or proprietary baby foods, which consist almost wholly of carbohydrate, are fed over an extended period of time. The milk is, as a rule, excluded entirely or given in markedly reduced quantities. The following case serves as an excellent example of how this disturbance is brought about: A. M. was first seen when five months of age, and the following history was obtained. The infant was born of normal parents, and was breast-fed until three months of age. Breast feeding was discontinued because of vomiting, and a lactic acid milk mixture was prescribed. After four weeks this mixture was discontinued because of failure to gain in weight, and a mixture consisting of 900 gm. of water, 50 gm. of malt soup extract, and 15 gm. of flour was ordered. The infant was given this mixture for one month until it developed diarrhea, when it was brought to my attention.

The infant at this time presented the clinical picture of the hypertonic-atrophic type of starch injury. Three types may be distinguished clinically: first, the hydremic type which occurs when salts are added to the starch feedings. The infants are edematous, pasty in appearance, and the musculature is doughy on palpation. The water fixation is imperfect and may be suddenly and rapidly given off at the slightest insult. The second is the atrophic type. The third is the hypertonic type. The muscles are rigidly contracted, the head is thrown backward, and the arms and legs are flexed and adducted; the rigidity is so marked at times that it may be mistaken for meningitis.

(*d*) Lack of accessory foodstuffs (keratomalacia, scurvy). Here the nutritional disturbance is accompanied by definite organic changes.

Quantitative inanition may be due to:

(*e*) The feeding of excessively dilute formulas.

(*f*) The feeding of well-balanced mixtures with an insufficiency of total calories. The insufficiency may be relative, *i. e.*, the number of calories may be sufficient for the infant's actual weight, but insufficient for what it should weigh.

(*g*) Vomiting (pylorospasm). The infant may be supplied with sufficient food in the bottle, but the amount that reaches the intestinal tract is insufficient.

2. **Dystrophy due to infections,** *e. g.*, furunculosis, pyelitis, chronic nasopharyngitis, etc. Anorexia practically always accompanies the infection and, at times, persists even after the infection has subsided. As a result, the immunity is further lowered, the infant becomes more susceptible to infections, the anorexia becomes more marked and constant, and a vicious circle is established. It is this type of dystrophy which is most often encountered and which proves most troublesome in the management.

3. **Dystrophy due to constitutional disturbances,** producing developmental retardation, *e. g.*, prematurity, erythrodermia desquamativa, cerebral anomalies such as Mongolian idiocy, and congenital cardiac disturbances.

As stated above, diarrhea may or may not accompany this

type of dystrophy. Treatment will depend not only upon the presence or absence of diarrhea, but also upon the type of diarrhea present. Diarrhea accompanying dystrophy is of three types:

1. **Fermentation Diarrhea.**—This type may result from:

(*a*) Feeding a mixture which is well balanced, but which exceeds the infant's tolerance. Here stasis occurs, and there is an upward migration of organisms into the duodenum where normally no organisms are found, and consequently abnormal carbohydrate fermentation occurs. Excessive fatty acids are produced which irritate the intestinal wall, causing increased peristalsis.

(*b*) Feeding a mixture of improper composition, *e. g.*, a mixture which contains too much sugar and too much whey.

2. **Inanition Diarrhea.**—This type occurs most frequently in the newborn. As a rule, an infant will react to starvation with constipation, but, if there is a tendency to water instability, diarrhea will occur. It is important to be familiar with this type of diarrhea because food withdrawal, which exerts a favorable influence on the first type, has the opposite effect here. Inanition diarrhea may also be due to qualitative inanition. Carbohydrate deficiency is usually the main factor, though a deficiency of vitamins or of fat and protein, as is encountered in "Mehlnährschaden," also results in diarrhea.

3. **Irritation diarrhea** may be:

(*a*) Infectious with structural changes in the mucosa (typhoid, paratyphoid, dysentery), or

(*b*) Parenteral or toxic, *i. e.*, caused by infections outside of the gastro-intestinal tract. The diarrhea which accompanies upper respiratory infections affords an excellent example of this type. The diarrhea frequently disappears when the infection subsides without the aid of special treatment, but it may persist until a proper dietetic regimen is instituted; or evidences of the infection may be slight and the diarrhea severe, so that the gastro-intestinal symptoms overshadow the infectious process which is then easily overlooked. It is this type of diarrhea which is most often encountered in the dystrophic infant.

It is frequently difficult to determine the type of diarrhea present. Differentiation between the fermentation and the irritation types is particularly difficult. In fact, the three types may occur simultaneously, affording additional difficulty in the differentiation.

Treatment.—*General Principles.*—Intelligent treatment is possible only when the etiology is clear. It consists in correcting the deficiency either qualitatively or quantitatively. Whether the deficiency can be entirely equalized at once will depend upon the presence or absence of diarrhea, and upon the infant's tolerance for food. If the disturbance is of long standing with a resulting break in the tolerance, it is best to begin cautiously, giving but small quantities of the therapeutic mixture indicated. The rapidity with which increases are made will depend upon the reaction of the infant. This holds true whether diarrhea is present or not. The volume of the mixture should be regulated to conform with the infant's ability to take food. The caloric requirement should be computed from the normal weight and not from the actual weight.

Treatment of Dystrophy Without Diarrhea.—Treatment is much simpler and is attended with greater success when diarrhea is absent. The missing elements in the diet may be supplied at once and in their proper proportion, except when the infant's tolerance is low, when it is three months of age or younger, or when the infant's weight corresponds to that of a normal three-months-old infant. When these conditions are present it is best to employ breast milk; if breast milk is not available, buttermilk cooked with $1\frac{1}{2}$ per cent. flour, with the addition of 5 per cent. dextrimaltose, should be used. It is best to begin with 300 c.c. for the first twenty-four hours, and to make increases of 50 to 75 c.c. daily until the infant receives 150 c.c. per kilogram of body weight. In dystrophy due to quantitative insufficiency, provided the tolerance is good, it is necessary only to increase the food intake to meet the caloric requirement. A gain in weight almost invariably follows. It should be kept in mind that many infants in this group will require 150 calories per kilogram of actual body weight. Rela-

tive to the qualitative insufficiencies: If the dystrophy is due to a lack of water, as when concentrated feedings are employed, the same mixture is continued and water is supplied between feedings to meet the infant's fluid requirement—1/6 to 1/7 of its body weight. If the disturbance is due to an avitaminosis, supplying the missing vitamins will give brilliant results. In scurvy the addition of lemon juice, orange juice, or tomato juice in 30 to 60 c.c. doses will produce a complete change in the clinical picture. In xerophthalmia the addition of cod liver oil or butter-fat to the diet will give excellent results.

The Treatment of Dystrophy Due to Carbohydrate Deficiency (Milk Injury).—In mild cases the following will give results: If the infant has been previously overfed, it is essential, first to reduce the number of feedings to 5 in twenty-four hours, and second to reduce the amount of milk so that the infant does not receive more than 100 gm. per kilogram of body weight. In place of water a cereal decoction prepared with oatmeal or wheat-flour should be employed as a diluent. Five to 7 per cent. cane sugar or dextrimaltose should be added to the mixture. In severe cases these measures will usually prove inadequate. One of two methods may then be employed:(1) Treatment with breast milk or, if this is not available, (2) treatment with a milk, flour, and malt-soup mixture. As stated above, breast milk is indicated in infants during the first three months of life. The total for the day should be 1/6 of the body weight, just as in the normal infant. Because of the low salt and protein content of breast milk, reparation takes place more slowly than when artificial feeding is employed. Improvement in the color of the skin, in the agility of the infant, in the turgor, and in the disappearance of restlessness, may occur even before a gain in weight is manifested. In spite of the failure to gain in weight, however, no change in the feeding regimen should be made. The stage of reparation may last from two to four weeks. It may, however, be shortened by substituting one or two bottles of a low fat and high carbohydrate mixture, *e. g.*, buttermilk with the addition of $1\frac{1}{2}$ per cent. flour and 5 per cent. dextrimaltose, for one or two breast feedings. When the infant is

making satisfactory progress, *i. e.*, after a lapse of another two or three weeks, an additional bottle may be substituted for a breast feeding, and so on, until the infant is entirely artificially fed.

When a milk, flour, and malt-soup mixture is employed, the total amount of milk for twenty-four hours should be less than 1/10 of the body weight. Wheat, barley, or maize flour decoctions are added to make up the fluid requirement of the infant. Malt-soup extract is employed because of its calcium carbonate and vitamin content. It is best to begin with 30 gm. for twenty-four hours, and to increase gradually until 60 gm. are given. With malt-soup extract the stools are brown, and the intestinal flora is of the same character as when breast milk is given. If the stools become too frequent, the malt-soup extract should be reduced. Keller's malt-soup mixture, which consists of 1/3 liter of milk, 2/3 liter of water, 50 gm. of flour, and 100 gm. of malt-soup extract, is particularly indicated in this type of dystrophy in older infants who, at the same time, manifest constitutional disturbances, such as spasmophilia, rickets, and exudative diathesis. These high carbohydrate mixtures should not be given for longer than five to six weeks. A change to a normal mixture should be made as soon as reparation is well advanced. Older infants may also be given carbohydrate in the form of gruel or zwieback, in addition to the malt-soup extract.

Treatment of Mehlnährschaden or starch injury may be instituted with artificial or breast feeding. When artificial feeding is employed, the starch mixture is not discontinued, small quantities of the mixture being replaced by cow's milk at first. In the preparation of the flour mixture it is advisable to employ a flour that does not ferment easily, *e. g.*, wheat, barley, rice, or maize flour. Because of the protein deficiency, protein in some form should also be added until milk can be supplied in adequate amounts. Thus on the first day of treatment 10 to 20 gm. of milk are added to each of the five flour feedings, and an addition of 15 gm. to each feeding is made each day, until the infant receives 1/10 of its body weight in milk. The flour mixture is decreased proportionately as the milk is increased. Sugar should be added cautiously at first; later it may be increased

to 5 to 7 per cent. At the beginning of the treatment 5 to 10 gm. of casec or larosan should be added; the protein preparation may be eliminated when the infant receives sufficient milk to cover the protein requirement.

Dystrophy due to repeated infections is practically always complicated by severe anorexia, and it is best treated with concentrated mixtures. Two-thirds milk with the addition of 8 to 10 per cent. carbohydrate, or whole milk with the addition of 10 to 12 per cent. carbohydrate, thick cereal feeding prepared with whole milk, Moro's whole milk butter-flour gruel, or Moro's whole milk butter-flour mixture will be of definite aid in producing a gain in weight. With these mixtures it is possible to feed a large number of calories in a small bulk, and thus achieve the gain in weight which is essential to increase the infant's resistance to infection. Only in this way is it possible to break up the vicious sequence of infection, anorexia, dystrophy, infection, anorexia, etc. Butter-flour whole milk gruel consists of 1 liter whole milk, 50 gm. butter, 70 gm. flour, 40 gm. sugar, and contains 1650 calories. Butter-flour whole-milk mixture consists of 1 liter milk, 50 gm. butter, 30 gm. flour, 70 gm. sugar, and contains 1560 calories. When concentrated feedings are employed, care should be observed not to exceed the infant's tolerance, and to supply a sufficient quantity of water between feedings.

If anemia complicates the dystrophy—and this is not at all uncommon when repeated infections are the etiologic factor—improvement will not take place until measures are instituted to combat the anemia. Ferrous carbonate, saccharated, in 10-gr. doses three times a day, is of value for this purpose. In older infants the effects of iron therapy may be enhanced by the addition of vegetables and calves' liver to the diet.

Treatment of Dystrophy with Diarrhea.—Treatment will depend upon the type of diarrhea present. If the diarrhea is due to insufficient food the diet should be increased rapidly to meet the caloric requirement regardless of the number of stools. In the irritation type no radical changes in the amount or in the quality of the food need be made, provided the general condition, as judged by the agility of the infant, by the color of

the skin, etc., is good. As a general rule, the diarrhea disappears with the subsidence of the infection. This is of special significance in dystrophic infants, because the institution of unnecessary starvation periods will aggravate the disturbance and result in further lowering the immunity. If it can be definitely determined that the diarrhea present is of the irritation type, the usual mixture may be continued, but it should be acidified with lactic acid or citric acid. In the fermentation type the total quantity of food must be reduced; qualitative changes will depend upon the severity of the general disturbance. Frequently it is impossible to diagnose the type of diarrhea present. Under these conditions it is best to institute a hunger period lasting from six to twelve hours, depending upon the degree of malnutrition present. If the infant is much below weight, protracted or repeated hunger periods are dangerous. Weak tea, sweetened with saccharin, is given during the hunger period to supply the infant's need for fluids. Small amounts of the therapeutic mixture are then given in frequent feedings, and rapid increases are made. If there is no change in the character and frequency of the stools, it is fairly good evidence that we are not dealing with the fermentation type. The amount of food may then be even more rapidly increased, so that the infant receives the same number of calories at the end of three days as it did before the hunger period was instituted. Then if there is a failure to gain in weight, additional carbohydrate should be added. However, it is best to employ carbohydrates that do not ferment easily.

The choice of a therapeutic mixture will depend upon the general manifestations. Three methods may be followed:

1. *Change in Carbohydrate.*—If sugars which ferment easily, such as lactose or cane sugar, have been employed, dextrimaltose or one of the flours may be substituted.

2. *Addition of Protein.*—Fifteen to 20 gm. of casec, larosan, or plasmon may be added to the day's feeding.

3. *Employment of Acidified Milks.*—(*a*) Buttermilk, cooked with $1\frac{1}{2}$ to 3 per cent. flour. Commercial buttermilk should not be employed. Buttermilk for infant feeding should be pre-

pared with a pure culture of lactic acid bacilli and should have a definite degree of acidity; 4.3 c.c. of N/2 sodium hydroxid should neutralize 25 c.c. of buttermilk. The results are better when the milk is acidified in this manner than when lactic acid, citric acid, or vinegar is used.

(*b*) *Protein milk* should never be employed with a carbohydrate addition of less than 5 per cent.

(*c*) *Citric-acid milk* (2 per cent. lemon juice) and lactic-acid milk (3 c.c. of lactic acid to 500 c.c. of milk).

At the beginning of treatment a short hunger period is instituted, as mentioned above. If the diarrhea is not severe, and the infant's general condition is fairly good, the first or second method may be employed. If the diarrhea does not subside and the child fails to gain after six to seven days of treatment, a change to the third method should be made. Under no circumstances, however, should another hunger period be instituted, nor should the acidified milk be given in reduced quantities. If protein milk is employed, 200 c.c. per kilogram of body weight should be given at once; if buttermilk, 150 c.c. per kilogram.

If the diarrhea is severe and the infant's general condition is poor when it is first presented for treatment, it is best to employ the third method. In young infants, buttermilk is indicated; in older infants, protein milk may be used. It is best to proceed as in the treatment of acute nutritional disturbances by instituting a starvation period of six hours, and then giving 30 c.c. of buttermilk or protein milk with 5 per cent. dextrimaltose ten times a day. The fluid requirement is made up by the administration of tea or a weak flour-decoction. Ten cubic centimeters are added at each feeding daily until the infant receives 200 gm. of protein milk per kilogram of body weight per day or, if buttermilk is used, 150 c.c. per kilogram of body weight for twenty-four hours. At this time the number of feedings is reduced to 5 or 6 in twenty-four hours. The increases must be made schematically and regularly, regardless of the character or frequency of the stools. If no gain in weight occurs when the infant is receiving its full quota of protein milk, the carbo-

hydrate content should be increased to 7 or even 10 per cent. At times a decrease in the number of stools does not occur until 10 per cent. carbohydrate is added. The protein milk is given for six to eight weeks, when a change to normal feeding is made. The change may be made gradually or at once. Lactic-acid milk, prepared with 3 c.c. of lactic acid to the ½ liter, and containing 5 to 7 per cent. carbohydrate, is the mixture of choice. Cereal and vegetables should also be added to the diet cautiously in infants over five months of age.

When buttermilk is employed it is not wise to increase the carbohydrate content above 5 per cent. To increase the caloric value of the mixture one of two procedures may be followed: (1) The buttermilk may be gradually reduced and protein milk substituted until the infant receives protein milk exclusively; or (2) butter-flour thickening may be added to the buttermilk mixture. The fat should be added cautiously, only 2 per cent. being used at first; later, it may be increased to 4 per cent. The thickening is prepared by melting a definite amount of butter, depending upon the percentage of fat desired in the mixture, adding an equal quantity of flour, and heating the mixture until it becomes brown and liquid. A small quantity of warm water, in which is dissolved the amount of sugar desired, is added; the whole is brought to a boil and then added to the buttermilk. Buttermilk with the addition of fat in this form may be given for an indefinite period. In fact, L. F. Meyer employs this formula routinely in all infants at the Berlin Orphan Asylum until the infants are six to seven months of age, when a change to whole milk is made. Cereal and vegetables are added at the usual time if the stools are normal. He attributes the striking decrease in the mortality rate in his institution during the last ten years to the fact that infants fed in this manner gain better and are less likely to suffer from nutritional disturbances, and, therefore, have a much greater resistance to infections. There has been a definite decrease in the number of cases of pneumonia, and the infants manifested greater combative power when the infection did occur (personal communication).

When anorexia is present it is frequently desirable to feed these mixtures in a more concentrated form. Concentrated protein milk with the addition of 20 per cent. carbohydrate may then be employed; or the protein milk may be cooked with farina and boiled down to a small volume.

The course of dystrophy may be complicated by the appearance of two symptoms which will frequently tax the physician's ingenuity to overcome. The first is vomiting and the second anorexia.

Vomiting disappears, as a rule, during the first few hours when food is withheld and only tea is given. If it persists, food should not be given by mouth, but hypodermoclyses or 10 per cent. glucose should be employed; 500 to 800 c.c. may be given in twenty-four hours by this route. In the meantime, the stomach is washed with saline once or twice in twenty-four hours.

Anorexia is commonly encountered in dystrophy, especially when infections are present. If the anorexia is mild, a policy of waiting is advisable. If it is severe, one of several procedures may be followed:

1. *A Change in the Technic of Feeding.*—The food may be given somewhat cooler than previously or it may even be given cold. The opening in the nipple may be made larger, or the mixture may be fed to the infant by spoon. A change in the posture of the infant during feeding time will occasionally give results. The number of feedings may be increased to 7 or 8 in twenty-four hours in young infants, or reduced to 3 or 4 in older ones. Finally, a change of nurse may be necessary.

2. *The Addition of Dilute Hydrochloric Acid.*—The addition of 8 to 10 minims of the dilute acid to the mixture just before each feeding (four to five times a day) will at times give good results. The administration of the acid is of value only when given in fairly large doses.

3. *Lavage.*—This method is particularly indicated if vomiting is present.

4. *Change in Type of Feeding.*—A complete change in the formula, *e. g.*, a change to a sweet milk mixture if acidified milk

has been employed, provided the stools are normal, will at times be followed by the desired results.

Finally, obstinate cases will be encountered, and then the employment of the fifth method, *catheter feeding*, will be necessary. The catheter, however, should not be employed oftener than twice a day.

CLINIC OF DR. HENRY M. FEINBLATT

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THREE CASES OF ENDOCRINE DISEASE WITH PRONOUNCED ASTHENIA

ONE of the most constant and distressing symptoms present in all serious disturbances of the endocrine function is progressive asthenia. This statement is exemplified by the histories of the following cases, representing diseases of the pituitary and adrenal glands and of the pancreas, respectively.

CASE I. DIABETES INSIPIDUS RELIEVED BY PITUITRIN

A white woman, thirty-two years old, married, and mother of two children, who complains of weakness, polyuria, polydypsia, insomnia, and great nervousness.

During the first week of February, 1926, she took care of a child ill with measles. At that time she developed an attack of "grippe," and was ill in bed for four days with fever, great fatigue, and pain in the back. Following this attack, the patient failed to recover her strength properly, and in April and May gradually developed irritability and began to fatigue rapidly. Her menses, which had previously been regular, ceased, and she has had amenorrhea ever since. On July 1st she developed a liking for water, which she never had before.

On July 15th, while on an automobile trip, she developed intense thirst and polyuria. Examination at that time showed the patient to be a well-nourished, well-developed, light-skinned, blonde female. The face was of the rotund type; skin, dry; hair, dry; the eyes reacted to light and accommodation; the fundi were negative. The mucous membrane of the mouth was dry, the tongue coated. Lung-bed clear, heart rate 65 to 70, sounds

clear. Thyroid gland slightly enlarged. The abdomen was relaxed and a little full, but essentially negative. The tendon reflexes were present, but the right knee-jerk was greater than the left. Blood-pressure, 110/80. Fluoroscopic examination and roentgenographic study of the head and chest were negative. Blood Wassermann was negative; red-cell count, 4,600,000; hemoglobin, 70 per cent.; white cells, 6000; polynuclear cells, 70 per cent.; small lymphocytes, 30 per cent. Chemical examination of the blood gave normal values.

Urea nitrogen was 12.0 mg.; uric acid, 2 mg.; creatinin, 1.5 mg.; sugar, 105 mg.; cholesterol, 150 mg.; and chlorids in whole blood, 470 mg. per 100 c.c. The urine was of a greenish color; specific gravity, 1002 (twenty-four-hour specimen). Single specimens during the day showed a variation of specific gravity between 1001 and 1003.

Weight, 125 pounds; height, 5 feet, 5 inches; temperature, 98.6° F.; pulse, 70.

Microscopic examination of the urine showed round cells; otherwise it was negative. The patient at that time passed between 6 and 7 liters of urine, and her thirst was unquenchable. She was placed immediately on hypodermic injections of pituitrin (Parke, Davis & Co. obstetrical preparation). The first dose given was 1 c.c. at night. The blood-pressure showed no change. This was followed by pallor of the skin and stimulation of the bowels. She became more restful and there was a marked diminution of thirst. The night output of urine after this injection decreased from $3\frac{1}{2}$ to 1 liter. The specific gravity rose to 1012, but the greenish pigmentation was still present. The dose was then decreased to 5 minims morning and night, with decided improvement in the patient's condition.

From September 1st to September 17th she was given 5 minims of pituitrin nightly. The urine concentration then rose as high as 1018.

On September 17th she developed a respiratory infection with a temperature of 101° F., and again had intense thirst which could not be controlled by this dose of pituitrin. She vomited all night and for two days thereafter. On September

21st she was given 4 minims of pituitary extract (not Parke, Davis & Co.). This was followed by marked cardiac depression. Medication was then discontinued and a salt-free diet given. Chlorid study of the blood and urine at that time showed no abnormal variation. Polyuria and polydypsia became very intense again, and with it there were insomnia, nausea, vomiting, and loss of strength. There was no quenching of thirst, as the patient was unable to retain any food or liquids. Examination of the eye-grounds showed the veins fuller than normal, with blurring of the upper nasal margins of the disks. The tendon reflexes were markedly exaggerated. There was marked loss of weight, and the patient was in a hyperemotional state. Pituitrin was resumed and resulted in rapid amelioration of the symptoms. The patient was given 5 minims at night and 3 minims in the morning, with prompt relief of the symptoms of nausea, vomiting, and thirst, and she returned to her normal mental and physical state.

From January to June, 1927 she was perfectly competent to carry on her duties and activites, and the pituitrin was decreased to 3 to 4 minims nightly. The taste for food returned, and the nausea and vomiting completely disappeared. The output of urine at that time had decreased to 3 liters in twenty-four hours.

Intranasal instillation of pituitrin was substituted every other day instead of the hypodermic. This was done by dropping 2 drops into each nostril below the inferior turbinate, after which procedure the patient gently sniffed it in. Larger amounts than 2 drops were absorbed with difficulty. Since August 1st the intranasal administration has been used entirely.

The urine during the first week of November showed a night concentration between 1015 and 1020, and a day concentration from 1002 to 1010. The night output has decreased to between 300 and 500 c.c.

Examination of the eye-grounds, and perimetric readings during November, showed increased blurring of the nasal disks, partial dipping, and temporal hemianopsia. More recent examination has shown a return to normal.

Weakness, amenorrhea, and insomnia were early manifestations. Polyuria, polydypsia, nausea, and vomiting followed. Pituitrin injections gave ready relief; other drugs, including the ovarian extracts were not effective. Salt-free diet gave no relief, and a study of the salt metabolism failed to show any evidence of faulty salt elimination.

Intranasal instillation by the drop method proved to be an efficient and practical means of administration for this small dosage.

The prompt and complete relief obtained with pituitrin strengthens the idea that this disease is due to pituitary hypofunction; namely, posterior lobe dysfunction. While the above syndrome of diabetes insipidus must be classified as a rare disease, milder types in which nervous symptoms predominate are relatively common.

In general, clinical recognition of pituitary diseases is made difficult by the inability of direct anatomical visualization of the gland itself, and by the fact that the secondary disturbances set up elsewhere often predominate in the picture.

As we acquaint ourselves with the clinical pictures of pituitary disease, we learn to appreciate that the condition is very common and probably as frequent as thyroid disease.

The disturbances of the function are either hyperactivity or hypo-activity. Emotional strains and toxins from unknown sources are important exciting factors.

Following continued excessive activity, there result morphologic alteration, with loss of secreting tissue, and a state of diminished function.

When hyperfunction comes early in life, gigantism results. When later, after epiphyseal ossification, there is a tendency toward acromegaly. If the deficiency occurs early in life, the Fröhlich syndrome results; if later, and after adolescence, the changes in the skin and sexual activity are the most obvious symptoms.

Milder types of these disturbances are frequently seen clinically in adults between the ages of twenty-five and forty, but are not uncommonly seen in the 'teens. There may be, in

younger individuals, a tendency toward overgrowth, enlargement of the hands and feet, and faulty sexual development, either excessive or diminished. In girls there may be delay, irregularity, or absence of menstruation. In adult women there are commonly a loss of libido, insomnia and abnormal craving for sweets.

In the absence of neighborhood and general pressure-symptoms, only few of these patients are incapacitated to any considerable extent.

CASE II. ADDISON'S DISEASE FOLLOWING VERTEBRAL TUBERCULOSIS

A man, fifty-nine years old, was brought to the hospital complaining of weakness, nausea, vomiting, and anorexia. He was first observed ten years ago for pain in the back. Examination at that time showed tuberculosis of the tenth, eleventh, and twelfth dorsal vertebræ. The lungs were negative. Blood-pressure: systolic, 115; diastolic, 75. Urine negative for tubercle bacilli. The local condition was treated with a plaster cast.

Present Illness.—Three months before admission he developed progressive asthenia and had to go to bed. Any effort to walk resulted in collapse. Vomiting began five weeks ago. At first it occurred only in the morning, but later increased to four or five times daily. He had no chills or fever.

Examination shows an elderly Italian, with white hair standing out in contrast with his dark-brown face; the eyebrows are black. The skin is frankly brunet, with deeper pigmentation of the hands, fingers, and toes. There are dark-brown blotches on the buccal mucosa. The spine shows lumbar angulation. Lungs, negative; extremities, thin; knee-jerks, diminished. Temperature, 99° F.; pulse, 84; respiration, 20. Blood-pressure: systolic, 100; diastolic, 84.

Ergographic test of digital flexor muscles shows a normal fatigue reaction with a lift of 2 to 3 and 4 kilos.

Laboratory Findings.—Urine: specific gravity, 1018, negative chemically and microscopically. Red cells, 4,800,000; white cells, 7200; hemoglobin, 96 per cent.; polynuclear cells, 49 per

cent.; small lymphocytes, 11 per cent.; large lymphocytes, 40 per cent. Blood-chemistry: urea nitrogen, 17.6 mg.; uric acid, 2.6 mg.; sugar, 105 mg. per 100 c.c. The condition became progressively worse, and the patient died five days after admission.

Autopsy.—The body was that of a well-nourished male. Rigor mortis had not yet developed. Some pigmentation was seen over the body, particularly on the fingers and chest, and in the axillæ, and on the buccal mucosa. A small cold abscess was seen in the skin over the sixth rib, and about 2 inches to the left of the midsternal line. This abscess extended into the rib, which was soft and necrotic. Both lungs were very adherent to the chest wall throughout. There was congestion, but no evidence of tuberculosis was found in the lungs. The pericardial sac was normal. The heart weighed 350 gm. The left ventricle appeared much shortened, and the left auricle enlarged. All valves were normal. The right heart was normal. The diaphragm was adherent throughout to the upper surface of the liver. The liver weighed 1600 gm. and showed passive congestion. Many adhesions were found around the gall-bladder. The spleen weighed 400 gm. and was adherent to the surrounding structures. The cut surface showed no gross lesions. The stomach and pancreas appeared normal. The left adrenal gland had lost its normal outline and appeared to contain isolated areas of caseation. The right adrenal gland was large and appeared to be a mass of caseation, no normal tissue remaining. The mesenteric and retroperitoneal glands were not enlarged.

Cause of death: Addison's disease.

Microscopic Examination: Myocardium, negative. Pancreas, negative. Stomach, negative. Kidneys, edema, congestion and marked cloudy swelling. Liver, congestion and hemosiderin. Adrenal, the normal structure has been entirely destroyed by the tuberculous process.

Comment.—The predominating symptoms were progressive asthenia, nausea, and vomiting. Pigmentation was the obvious physical finding. Chemical examination showed normal blood-sugar. There was no obvious disturbance of fat metabolism. Systolic blood-pressure was not strikingly low. Pulse pressure

was as low as 16 mg. Hg. The hemoglobin and the cytology of the blood were well within the normal. While the symptomatic asthenia was great, the actual power of the voluntary muscles to do work was equal to normal. The course of the disease here is hard to determine, but the condition was already established three months prior to entrance.

Necropsy findings showed active bone-tuberculosis, and destruction of the entire adrenal structure. In this case there was whole gland deficiency. No other definite pathologic changes were noted.

CASE III. DIABETES MELLITUS (JUVENILE TYPE) IN AN ELDERLY WOMAN

A woman, fifty-nine years old, was brought to the hospital complaining of progressive weakness, polyphagia, polydypsia, and loss of weight. She had been in the hospital one year before for the same condition, at which time she responded to routine treatment for diabetes and was discharged improved.

While under observation, she lost rapidly in her tolerance for food in spite of dietetic and insulin treatment, and again developed severe symptoms of diabetes. She was advised to enter the hospital for study.

Examination showed an emaciated, gray-haired, elderly woman, who was acutely ill. Her breath smelled strongly of acetone; the tongue was parched, and the mucous membranes dry and pale. The patient responded slowly to questioning, but was mentally clear. The thyroid gland was palpable, chest sunken, breasts atrophied. The heart was hypertrophic. The abdomen was scaphoid, and there were tenderness of the right upper quadrant and fulness of the gall-bladder. The extremities were poorly developed. The tendon-jerks were absent. There were thickening and tortuosity of the larger blood-vessels.

Laboratory Examination.—Blood-sugar, 375 mg.; urea nitrogen, 42 mg. per 100 c.c.; urinary sugar, 4 per cent.; ketone bodies, present. Van Slyke CO_2 combining power was 20.

She was given, in the course of a day, 145 units of insulin, with very little effect on the sugar content of the blood or urine.

The following day she received 265 units in addition. This dosage was kept up for the first week with marked improvement in the general condition, and reduction but not clearing of the glycosuria. She was then placed on a diet of protein, 70 gm.; fat, 90 gm.; and carbohydrates, 180 gm., and was given 80 units of iletin three times a day.

At that time her blood-sugar was 390 mg.; urinary sugar, $3\frac{1}{2}$ per cent.; ketone bodies, present. The food intake was reduced to: proteins, 50; carbohydrates, 120; and fat, 50 gm. Insulin dosage was reduced to 190 units daily. The acidosis on this regimen became more severe, and the insulin dosage had to be raised to 210 units daily for the next two weeks. During that time the blood-sugar persisted between 250 mg. and 350 mg., and the urinary sugar between 2 and 3 per cent.

Any attempt to increase the dosage of insulin above this figure resulted in symptoms of insulin shock; that is, the patient would develop generalized twitchings, become dazed, and finally lose consciousness at times for as long as an hour.

In spite of the treatment, hyperglycemia and acidosis continued. The patient developed bronchopneumonia and died.

This case illustrates what may be called an acute exacerbation of chronic diabetes, in which carbohydrate tolerance drops to practically zero, and in which asthenia and emaciation are the most disturbing symptoms. It is interesting to note that large doses of insulin failed to control the intolerance for sugar, and that symptoms of insulin shock were produced without hypoglycemic findings.

Necropsy.—The body was that of a thin old woman. The liver weighed 1260 gm. It was brownish-yellow in color. The cut surface was fairly dry and shiny. Microscopic examination showed an excessive amount of fatty infiltration; otherwise it was negative. The spleen weighed 220 gm. It was soft. Microscopic examination was essentially negative. The kidneys weighed 220 gm. each. The surface was slightly granular; the capsules stripped easily. The cut surface showed normal medullary markings. Microscopic examination: glomeruli normal, cloudy swelling of tubular epithelium. There was marked

sclerosis of the arteries. Adrenals of normal size; normal microscopically. The pancreas was small, very firm, and grayish-yellow in color. Microscopically there was marked general decrease in island tissue, the remaining islands showing patches of hyalin deposit. The fibrosis was increased throughout.

The left ventricle was hypertrophied; otherwise the heart was negative. The aorta and abdominal vessels were dilated, tortuous, and thickened. The aorta showed evidence of atherosclerosis. Scattered throughout both lower lobes of the lungs were small areas of consolidation. The microscopic examination showed evidences of bronchopneumonia. The gall-bladder was distended and contained stones.

Pathologic Diagnosis.—General arteriosclerosis, bronchopneumonia, diabetes, atrophy of pancreas, and gall-stones.

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THE CLINICAL TYPES OF CARDIAC FAILURE

WHEN the heart is subjected to the influence of disease or excessive labor, and functions beyond its powers in consequence, it endeavors to compensate for the overload, absolute or relative, by the development of hypertrophy, with which a certain degree of dilatation is usually associated. In the event that this compensation is not adequate, cardiac failure develops. In the words of Mackenzie,[1] cardiac failure is the "inability of the heart muscle to maintain an efficient circulation," and he adds that this failure is due to some impediment embarrassing the work of the heart muscle or to some defect in the heart muscle itself.

The etiology of cardiac failure cannot be so simply considered, however, for while pre-existent cardiovascular disease and overexertion are the more important factors, reinfection of the endocardium and the toxic effect of chemical poisons play a part in some of the cases. Barringer's[2] study of 154 patients established the influence of endocardial reinfection beyond argument. Of his cases: 117 had fever; 69 had polymorphonuclear leukocytosis; 7 only had experienced physical or mental strain, and of these, 6 had fever and 3 leukocytosis. The influence of industrial chemical poisons on the heart muscle is a matter for further observation and study: phosphorus and ethyl-lead particularly are under suspicion.

Pre-existent cardiovascular disease, valvular or muscular, has lessened the power of the heart muscle through the medium of definite pathologic changes, these being either gross or micro-

scopic defects, the results of Aschoff or Bracht-Waechter bodies, replacement fibrosis, or fatty deterioration. Malnutrition, as in anemia, tuberculosis, and diabetes, participates in the development of these tissue changes, but more common are the influences of bacterial embolism, mural thrombosis, toxins of chemical nature, and senile factors.

The immediate outcome of the failure of the heart muscle is poor peripheral circulation, and the resulting modified physiology of the cardiovascular system is manifest in many organs and tissues of the body, according as these parts are supplied by the laboring heart. If the left ventricle is affected, the result is improper functioning of the systemic arterial system with tissue anemia; if the left auricle, there is stasis in the pulmonary blood-vessels with edema of the lungs and cyanosis; if the right ventricle and auricle are involved, there are cyanosis, general edema, and stasis in the portal circulation. In failure of severe type, there is a summation of the above.

When overexertion plays the prominent part in causation, the "reserve force" of the heart is exhausted by the overstrain, and the phenomena of decompensation ensue as a natural and unavoidable result.

The **onset of cardiac decompensation** may be slow, subtle and insidious, with fatigue, gradually developing dyspnea on exertion, and precordial pain, going on to edema; or it may be sudden, with faintness, vertigo, pain in some cases, with sense of impending death, or death itself. Obviously, there are intermediate cases.

The **causes of slowly developing decompensation** are the myocardial changes above referred to, with chronic focal infection contributing to the pathology in the myocardium, valvular defects leading to hypertrophy with new and revised muscle-power of the various heart units, adherent pericardium with its sometimes extraordinary cardiac hypertrophy, obesity with its far-reaching effects in accomplishing imbalance, the deteriorative influence of syphilis, chemical poisons like phosphorus and alcohol, remembering the emphasis which Osler placed upon beer especially, overexertion as in the chronic stair-climber, and

visceral lesions elsewhere in the body. I refer particularly to asthma, old tuberculous lung fibrosis, emphysema, chronic bronchitis, and spinal deformities with changed intrathoracic relations, all influencing the right side of the heart; and aortal disease, arteriosclerosis, and chronic nephritis, particularly leading to embarrassment of the left ventricle. In the case of exophthalmic goiter and toxic adenoma a special metabolic poison influences the cardiac and vasomotor system.

Acute cardiac decompensation, often so unhappily dramatic, has for its chief causes: rapidly forming large thrombi in the cavities of the heart, blocks in the coronary system (embolic or thrombic in character), rapidly increasing pericardial effusion, rupture of the heart muscle or spontaneous rupture of a valve, bacterial poisons (as in diphtheria), overactivity of the vagi at any point in their course from their centers to their end terminals in the heart wall, and "acute indigestion" with upward displacement of the diaphragm.

The **symptoms of heart-failure,** always entirely subjective at first, are variable. Some are readily explained, but others are difficult to account for. Dyspnea, constant or paroxysmal, is the outstanding feature of the decompensation status, and is due largely to the fact that the respiratory center in the brain is not receiving sufficient blood. There are other causes that may contribute physically: stasis in the lung tissue, fluid at the lung bases, and decreased vital capacity. Precordial distress and oppression are reflex arc symptoms from the struggling heart-muscle. Anorexia, vomiting, gastric flatulence, and pain are due to congestion and stasis in the blood-vessels of the stomach wall, while poor cerebral circulation further accounts for vertigo, throbbing headache, mental depression, and failure to mentally concentrate. Constipation and diarrhea are the result of changes in the tonicity and wall of the lower bowel, and pain in the right hypochondrium is due to liver congestion with stretching of Glisson's capsule.

The **signs of heart-failure** depend upon the degree of the decompensation, and may be divided into those of beginning failure and those of complete failure:

1. *Signs of beginning failure.*
   - Dyspnea on exertion, slight to moderate; occasionally orthopnea.
   - Cyanosis on exertion.
   - Rapid heart, sometimes irregular; enlarged to left.
   - Enlargement and tenderness of liver; sometimes spleen.
   - Râles of moisture over the lung bases, with dulness on percussion and decreased breath-sounds.
   - Occasionally slight icterus.
2. *Signs of complete failure.*
   - Constant dyspnea, frequently necessitating Alpine climber's posture.
   - The breathing may be Cheyne-Stokes in type.
   - Cyanosis of lips and fingers; nostrils dilating, skin cold, clammy, and often yellowish.
   - Frequent short cough with tracheal rattling; sputum often blood-streaked.
   - Heart: Dilated in all directions with diffuse, wavy apex impulse. Murmurs fainter than usual or disappeared. Relative mitral and tricuspid regurgitation may develop, the latter with pulsating liver. The heart is rapid and total irregularity of action is present, with a low blood-pressure, pulse deficit, and dilated neck veins.
   - Edema of feet and legs, external genitalia, abdominal wall; "lumbosacral pillow" if patient is in bed may be the only evidence; occasionally, edema of dependent arm.
   - Passive congestion is everywhere present, with hydrothorax, ascites, sometimes bloody diarrhea.
   - The urine may show albumin and casts. The low reading of the phenolsulphonephthalein test does not mean nephritis in the presence of cardiac decompensation.
   - A psychosis may be evident.

Concerning Classification.—The great majority of text-books, if they refer at all to the matter, speak of only two forms of decompensation: namely, congestive failure and anginoid failure. We can go to the other extreme and create types and subtypes to the point of utter confusion. It would seem, however, that

there would be a distinct value in a classification which, through recognition of the etiologic factor or of some dominant feature of the failure, would classify the types in our minds and lead to a more understanding therapeutic attack. All classification is dogmatic to a degree; to offset this, some advantage must accrue.

We have been extraordinarily indebted in the past to the Boston cardiologists for the emphasis placed by them upon the etiologic grouping of cases of heart disease (rheumatic, syphilitic, arteriosclerotic, goiter, etc.), and one is tempted to endeavor to apply this to the classification of heart-failure cases, but it seems advisable and more helpful to approach the subject from the clinical aspect and *group with regard to the outstanding feature of the failure.* The etiologic factor cannot be dismissed entirely, however, as will be seen.

The classification is as follows:

I. *Symptomatic type without edema or fibrillation.*
II. *Congestive failure type.*
    1. *Usual type with edema and rapid pulse, often in fibrillation.*
    2. *Chronic edematous type with slow heart; fibrillation present or absent.*
III. *Type secondary to thyroid toxicosis.*
IV. *Hypertensive type complicated with nephritis or arteriosclerosis.*
V. *Anginoid type.*
VI. *Type digitalis-proof.*
VII. *Sudden absolute failure type.*

I. **Symptomatic Type Without Edema or Fibrillation.**—We do well to be on the alert for cases in this group, as they often are undiagnosed for three reasons: they reluctantly seek the office of the physician, the symptoms are meager, and the findings upon examination are few. At most there are slight to moderate dyspnea and slight to moderate increase of the pulse rate; occasionally there is a slight throaty cough. A rest of a very few minutes suffices to restore the patient to ease and comfort. The examination reveals nothing definite; the heart

sounds are not vigorous, there is no arhythmia, there are no evidences of pulmonary, peripheral, or hepatic stasis, and there is often no murmur. The apex is a little to the left, but as the patients are often in the fifth decade this is of itself not surprising.

Upon study, the electrocardiograph may be revealing as to ventricular preponderance and restricted height of the amplitude.

Illustrative Case: A. G., Forty-five, Female, White.—Admitted to Methodist Episcopal Hospital, August 16, 1927, with history of a "nervous breakdown" seven years before, with prostration, weakness, and poor circulation, and lobar pneumonia last March. In early July, 1927 had slight attack of pleurisy. Since then weakness, palpitation, occasional swelling under eyes, and edema of feet, ankles, and hands.

Physical examination revealed no findings bearing on condition. Blood: red blood-cells, 4,630,000; hemoglobin, 80 per cent.; white blood-cells, 6900; 64 per cent. polymorphonuclears. Urine: negative. Phthalein tests: 30 per cent. first hour, 28 per cent. second hour: total 58 per cent. Wassermann and Kahn tests negative. Blood chemistry: negative. Pulse: 80 to 86 per minute. *x*-Ray: thorax 24 cm.; heart, 11 cm.; aorta, 5 cm.

The heart showed slight muffling of first sound at apex, second sound being accented slightly but definitely; the first sound over the aortic area was very distant. Blood-pressure 110/65 mm. After slight bending exercise, the pulse of 80 rose to 120, returning slowly to 88 in seven minutes. No murmurs were heard.

The electrocardiogram revealed irregularity of the ventricular complexes, and left ventricular preponderance.

Course.—Rest and sodium cacodylate slowly improved the patient's condition, and she left September 17th much improved.

II. **Congestive Failure Type.**—1. While this is the *usual type* characterized by dyspnea, edema of the extremities, moisture at the lung bases, and rapid, often irregular heart action, there are features which may mislead in the early cases of slight degree. I refer to coughing, wheezing respiration, gastric indigestion

with eructations and distress, loss of weight when the average case gains because of the fluid accumulations, tender liver suggesting gall-bladder disease, and pulmonary hemorrhage. Need I mention the cases of mitral stenosis considered tuberculous, the cases of early decompensation hurriedly operated for cholecystitis, the misdiagnoses of gastric cancer, or the cases of asthma that prove cardiac rather than bronchial?

The situation is cleared of possible doubt if the physical examination is searching enough, for the size of the heart, the altered balance of the heart-sounds, the presence of valvular

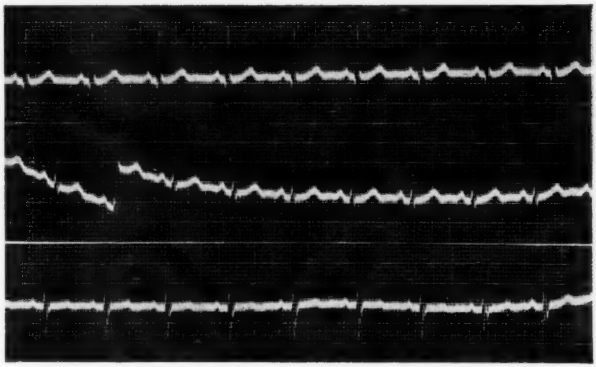

Fig. 169.—Electrocardiogram of A. G. (Symptomatic type without edema or fibrillation.)

defects and irregularity, the identification of a swollen or pulsating liver, the presence of ascites or pleural transudate all point to the cardiac origin of the symptoms.

Illustrative Case: G. P. G., Forty-six, Male, White.—Admitted to Methodist Episcopal Hospital, August 26, 1927, with history of rheumatic fever nineteen months ago, for which he was in bed seven months. He then returned to work feeling weak, and one month later began to have swelling of feet, ankles, and scrotum. In bed four months under medical care; edema disappeared, and he again returned to work six months ago. One month ago he went away on his vacation, from which he

returned with dyspnea, palpitation, edema, and precordial pain. He has been in bed now for three weeks with medical attention for the past few days only.

Physical examination revealed an enormously enlarged heart, with thrill and systolic murmur transmitted to left. Marked edema of both legs, enlarged and pulsating liver, and dilated and pulsating neck veins. Dyspnea and orthopnea. Electrocardiogram revealed auricular fibrillation; T_2 and T_3 are both downwardly deflected. The amplitude in all leads is decreased moderately.

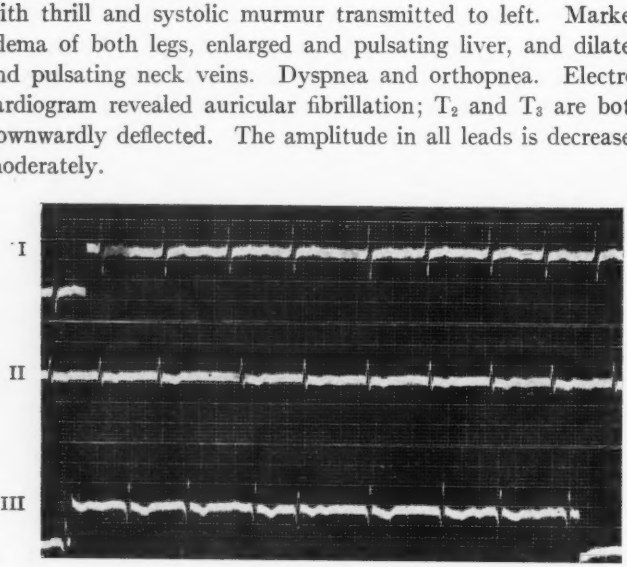

Fig. 170.—Electrocardiogram of G. P. G. (Congestive failure type: usual type with edema and rapid pulse, often in fibrillation.)

Course.—Forty-seven days in hospital. Progress of improvement steady; digitalis until pulse was slowed, and then, fibrillation persisting, quinidin in large doses to establish regular rhythm. Discharged October 10th. (Action still regular November 25th.)

2. There is a *chronic edematous type* with slow heart, fibrillation being present or absent, that is seen occasionally. Resistant to treatment, it gives evidence of involvement of tissues other than the heart. The illnesses of the type are long-protracted, with periods of improvement, but the edema is never lost entirely. In contrast to the digitalis-proof group (Type VI), the pulse remains consistently slow.

Illustrative Case: A. V. T., Forty-nine, Male, White.—Admitted to Methodist Episcopal Hospital, May 11, 1927, with history of chronic cardiac disability for two years. Chronic edema of the legs and dyspnea on exertion have been his only symptoms, but has been unable to work. He was in this hospital during the period of November 21 to December 26, 1926 for chronic myocarditis and cardiac hypertrophy. One week ago he had severe upper thoracic pain, radiating down left arm; he feared he was about to die. The attack lasted two days, and was diagnosed as coronary thrombosis. Thereafter the edema and dyspnea increased.

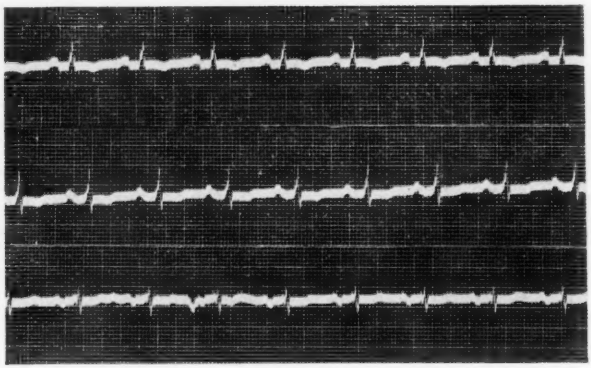

Fig. 171.—Electrocardiogram of A. V. T., May 13th. (Chronic edematous type with slow heart; fibrillation present or absent.)

Physical Examination.—Large man, weighing 203 pounds, rather orthopneic, and somewhat cyanotic. Heart, 14 cm. to left, 5 cm. to right. Sounds of poor quality and distant. No murmurs or irregularities. Lungs clear, no râles. Edema of extremities moderate. Electrocardiogram, normal rhythm, low amplitude in all leads, especially III. Abnormal ventricular complexes, especially up-arm of R-wave. P-waves show broad summits and P_3 is diphasic. P-R time is maximum of 0.20 sec.

Course.—Edema and dyspnea increased, and on the night of May 25th embolism occurred in the left lung, with the classic

symptoms of sudden pain in the chest, spitting of blood, and moderate fever of 102° F. Fluid later developed at the left base and, on July 11th, 500 c.c. were drawn off. Edema varied from time to time, depending upon treatment. He left the hospital November 16th, apparently to remain a chronic invalid.

III. **Type Secondary to Thyroid Toxicosis.**—A division devoted to this type is warranted because of the underlying cause, without recognition of which an ultimate good result in treatment may not be achieved. Tachycardia, frequently with fibrillation, with open flushed skin, overactive sweat glands, fine tremor, the well-known ocular signs and an appreciable thyroid tumor characterize this type. The basal metabolic rate is beyond +10 per cent., usually +20 to +40 per cent.

Unquestionably these cases are creating more interest than formerly for two reasons: because frequently the thyroid factor is masked and discoverable only after the closest clinical survey; and because the therapeutic attack is many times a matter of discussion between surgeon and physician. It is obvious that treatment should be individualized. If the hyperthyroidism is not marked, rest, special feeding, digitalis, and Lugol's solution may correct the condition. If the thyroid disease is severe, the medical treatment should be only preliminary to surgical correction of the thyroid disease. The presence of auricular fibrillation does not modify the treatment particularly, for digitalis and Lugol's solution continue to be indicated. As a step in preparing a toxic case for operation, Lugol's solution is a happy choice; dosage: 5 to 10 to 15 drops after each meal. The case is ready for operation when the pulse has dropped substantially, as invariably happens when the basal metabolic rate has come down 20 to 30 points, and when it is evident that the patient is on a wave of improvement clinically.

Illustrative Case: A. W. F., Fifty-eight, Male, White.—Admitted to Methodist Episcopal Hospital, May 9, 1927, with history of ten weeks of nervousness, tremulous writing, weakness, exhaustion, failure of appetite, loss of 35 pounds weight, rapid heart-action, intestinal flatulence.

Physical examination revealed auricular fibrillation. The

x-ray showed: thorax, 27.5 cm.; heart, 13 cm.; aorta, 5.5 cm. The basal metabolic rate was 54 per cent. The Wassermann and Kahn

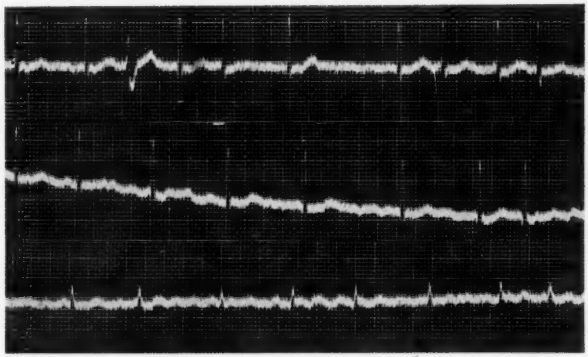

Fig. 172.—Electrocardiogram of A. W. F., May 9th. (Type secondary to thyroid toxicosis.)

tests were negative. Blood-count: red blood-cells, 3,750,000; hemoglobin, 68 per cent. Phthalein test: first hour, 26.2 per cent.;

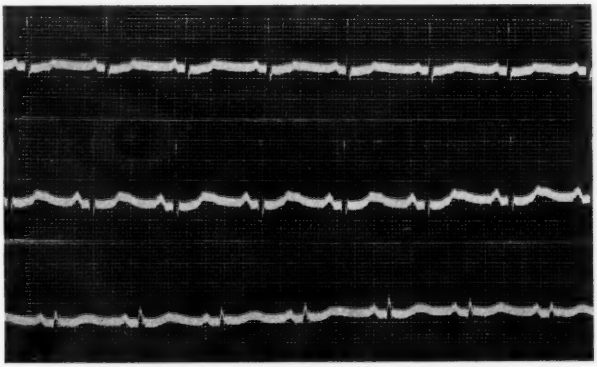

Fig. 173.—Electrocardiogram of A. W. F., May 19th. (Type secondary to thyroid toxicosis.)

second hour, 30 per cent.; total, 56.2 per cent. The urine was negative. Blood-sugar, 104 mg. Blood-pressure, 148/68 mm. The electrocardiogram showed auricular fibrillation.

Course.—Prompt response to moderate doses of digitalis up to a potential of 250 minims. A second electrocardiogram on May 19th revealed normal rhythm with widening of T_2.

Continued Course.—A. W. F. left the hospital May 25th, and at home was placed on Lugol's solution in preparation for operation. On June 20th he was operated at a sister hospital, made a splendid convalescence, now, on November 15th, weighing 184 pounds. He has regained all the weight lost, and is able now to undertake all professional duties. His heart-action is normal, and the electrocardiogram of November 7th is appended.

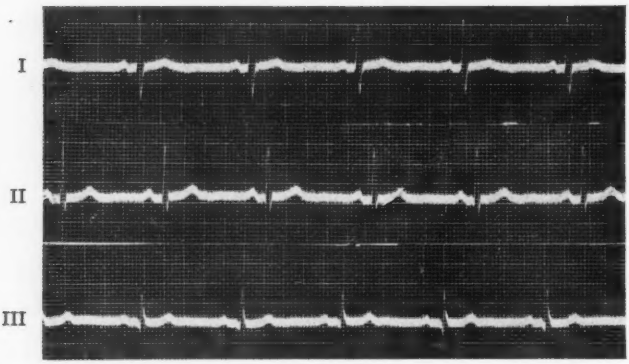

Fig. 174.—Electrocardiogram of A. W. F., November 7th. (Type secondary to thyroid toxicosis; recovered.)

IV. Hypertensive Type Complicated with Nephritis or Arteriosclerosis.—In this group the symptoms of decompensation, at first slight and purely subjective, gradually become more severe, so that dyspnea develops with the slightest exertion. The outstanding characteristic symptom, however, is an attack of nocturnal dyspnea, coming on abruptly between midnight and 3 A. M. and associated with pulmonary edema and the raising of large amounts of pink or red serous fluid. The attack is most dramatic, there being no warning. The patient, usually over forty years of age, wakes from his sleep gasping for breath and coughing up this pink serum in large quantities. He is mani-

festly in shock with cold wet extremities and brow. The pulse is weak and rapid. Recovery from the attack appears impossible, but within from one-half to one hour, especially if morphin has been given promptly, the attack has subsided. Death may occur in the attack, but it is not the rule.

These cases are uniformly high blood-pressure patients, with large hearts showing considerable dilatation as well as hypertrophy. There is usually associated nephritis. Ultimately these patients may develop true congestive decompensation.

Unquestionably Stengel's[3] cases of "paroxysmal pulmonary edema" fall in this group, for with one exception all were cases of cardiac, renal, and arterial disease, attended with high blood-pressure, and in this one exception mitral stenosis was present. Riesman[4] in his 1907 paper on acute pulmonary edema included some cases of this type.

The "*cardiac asthma*" cases of Pratt,[5] 39 in a series of 313 cardiac patients, form the basis of an interesting narrative of paroxysmal dyspnea and suffocation; when the attack was severe pulmonary edema to some extent was present. It is advisable to place "cardiac asthma" in this hypertensive type of failure.

Illustrative Case: C. B., Sixty-four, Male, White.—Admitted to Methodist Episcopal Hospital August 15, 1927, with a history of shortness of breath, flatulence, and abdominal distress for one year.

Physical examination showed enlarged heart, regular, except for occasional extrasystoles, no murmur. Blood-pressure: 180 mm. systolic, 140 mm. diastolic. Dyspnea of irregular type (Biot), with periods of hyperpnea and apnea, not rhythmical. Blood urea nitrogen, 20.75 mg. Phthalein test: two-hour total, 21 per cent. Urine showed albumin and hyalin casts. Ankles slightly edematous; liver enlarged and hard. *x*-Ray revealed: thorax, 24.5 cm.; heart, 17 cm.; aorta, 6 cm., transversely at two-meter distance. Blood: red blood-cells, 5,050,000; hemoglobin, 85 per cent.; white blood-cells, 8100; polymorphonuclears, 81 per cent. The electrocardiogram revealed left ventricular preponderance, with extrasystoles arising in the left ventricle.

Course.—Several attacks of typical nocturnal dyspnea. Sudden death on sixty-second day of hospital residence.

V. **Anginoid Type.**—This form is one which without doubt has increased in the United States during the past decade. It may not be strictly associated with structural change in every case for there are great differences of opinion as to the cause of angina pectoris, but the group of symptoms is outstanding, and commanding attention. It is associated in some cases with aortitis, luetic or arteriosclerotic in origin, or with aortic regurgitation of arterial type.

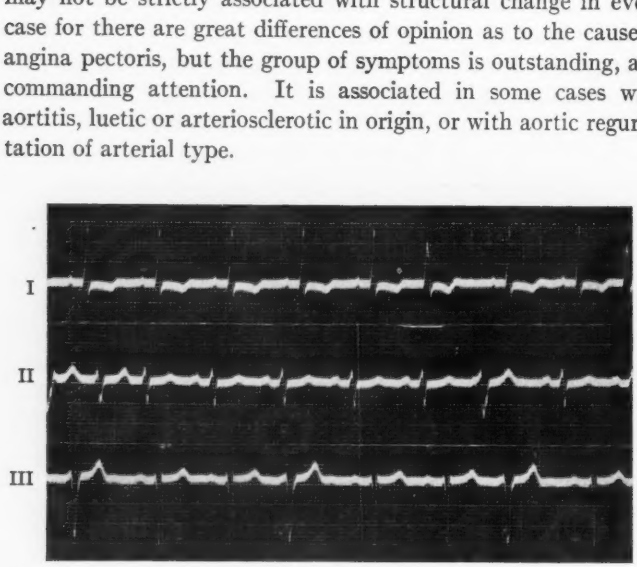

Fig. 175.—Electrocardiogram of C. B. (Hypertensive type complicated with nephritis or arteriosclerosis.)

The ease with which typical pain can be provoked provides the basis for further clinical subgrouping. Suffice it to say that physical exertion or emotional stress is the activating influence, and the dominant symptom, pain in the chest. Clutching, crushing pain directly in the breast bone, almost never in the heart region, extending into the arms, the neck, even the lips, is pathognomonic. Exercise is the acid test, and increasing sensitiveness to the exertion, be it muscular or psychic, is its chief characteristic.

We must be on the alert for the early cases, and go carefully into the history of all precordial pain, no matter how brief its

duration. "Pseudo-angina pectoris" has gone the way of "intercostal neuralgia." Nearly every case of heart cramp is real and not functional.

In this group fall the cases of coronary thrombosis. Severe structural damage often results from this mishap, and convalescence is a matter of weeks and months, with life activities ultimately on a 50 per cent. plane. The pain is abrupt in onset, although there may be invasional but misleading symptoms attributed to gastric or gall-bladder upsets. There is invariably slight fever and a moderate polymorphonuclear leukocytosis.

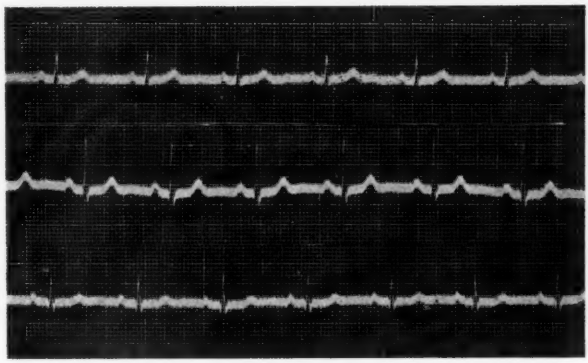

Fig. 176.—Electrocardiogram of A. E. (Anginoid type.)

The electrocardiogram often shows a slowly falling right arm of the R-wave (Pardee's sign).

Illustrative Case: A. E., Fifty-two, Female, White.—First office call December 24, 1926, complaining that beginning four months ago there was substernal pain on walking up hill or on the level. Previously for several months she had experienced slight but definite discomfort on walking up moderate hills. Recently 1 to 3 attacks daily.

Examination revealed average build, 5 feet 3½ inches, 134 pounds. Heart: enlarged slightly to left; slow heaving impulse at apex; no murmurs or irregularity. Blood-pressure, 200/105 mm. *x*-Ray: thorax, 25 cm.; heart, 12.9 cm.; 4.2 cm. to right,

8.7 cm. to left; aorta, 5.2 cm. Electrocardiogram: normal rhythm and rate, all R-waves dominate, no ventricular preponderance, ventricular complexes normal.

Course.—In January and April there were two nocturnal attacks of pain, awaking patient from sound sleep, and characterized by pain down left arm, weakness, and cold, pale face, with sweating. On modified activity and diuretin progress has been satisfactory. Weight has increased a few pounds, and attacks of substernal pain are now infrequent (every three to six weeks) and only after undue exertion. Blood-pressure 162/78 mm. (Last report October 3, 1927.)

VI. **Type Digitalis-proof.**—I add this group, because clinically the cases comprising it present one of our greatest problems in cardiology. Rest and digitalis are the main weapons in our hands in the treatment of heart disease. In fact, one classification of cardiac failure might be: (1) cases responding to rest and digitalis; (2) cases not responding. Every clinician sees these cases, and is puzzled, for the next therapeutic move is not clear.

These cases unquestionally have another factor besides decompensation, and that factor is either reinfection of the endocardium, or the presence of unsuspected disease elsewhere in the body. Enlargement of the spleen suggests bacterial activity, even though the temperature curve and leukocyte study do not present strong supportive evidence. Adhesive pericarditis is to be suspected in some of these cases, particularly if the heart is very large. In this group the pulse continues rapid, in spite of digitalis, and it is this pulse rate that sets them apart from the cases considered as chronic edematous type with slow pulse: fibrillation present or absent (Type II, subgroup 2).

Illustrative Case: W. M., Eighteen, Male, White.—Admitted to Methodist Episcopal Hospital, August 1, 1927, with history of tachycardia and palpitation at intervals since rheumatism at six years of age. Rheumatism each year since first attack. Acute cardiac failure developed two weeks ago with vomiting, shortness of breath, palpitation, precordial pain, and edema of legs.

Physical examination showed a huge heart, 12 cm. to left in sixth; space rate, 115. Diffuse, heaving impulse, action regular.

Systolic and diastolic murmurs and thrill at apex, and aortic regurgitation. Harsh to-and-fro rub over third left interspace. Liver enlarged. Edema of legs. Blood-pressure, 120 mm. systolic, 80 mm. diastolic. Red blood-cells, 5,800,000; hemoglobin, 78 per cent. Urine, albumin and casts. Phthalein tests, 0. Blood-chemistry, normal. Wassermann and Kahn tests, negative. No electrocardiogram taken.

Course.—Death in thirty-one days. No response to digitalis up to 475 minims potential. There was no autopsy.

VII. Sudden Absolute Failure Type.—Invariably the form of failure that comes to the mind of the laity when "heart disease" is mentioned; this is the rarest type of all in the practice of most physicians. Cardiac thrombosis plays an important rôle in its causation, fibrinous clots in a heart cavity becoming too large and impinging upon or plugging the valve orifices. Fragments of the clot may be loosened, and driven into the coronary artery openings, or be carried to brain, lung, kidney, or spleen, with fatal results.

When there is marked cardiac dilatation, there is increased likelihood to thrombus formation, and it is in these large hearts in fibrillation that Lewis[6] and others warn against the use of quinidin.

Great fear, anxiety, and anger have often lead to sudden death in heart disease. We do not always have the privilege of a necropsy, but the negative findings in some cases suggest a vagal influence. The conduction system is not proof against fatal insult, and may be responsible for some of these deaths.

In diphtheria, abrupt death after sudden exertion or excitement is associated with extensive degenerative myocarditis, although, in her 19 cases, Mathilde Loth[7] found persistently no true inflammation, but cloudy swelling and fat accumulation.

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CLINIC OF DR. S. R. BLATTEIS

JEWISH HOSPITAL

ENDEMIC TYPHUS FEVER (BRILL'S DISEASE). A REPORT OF 138 CASES

WHILE typhus fever, since Brill's description in 1898, can be readily divided into endemic and epidemic varieties, their discussion in the text and reference books is surprisingly disproportionate, endemic typhus receiving but scant mention, while all the emphasis is directed to the epidemic variety. To the student's mind typhus fever is associated with such terms as ship-fever, jail-fever, camp-fever, hospital-fever, etc.; a most serious disease, present in wide-spread epidemics, characterized by a profound clinical course, and with a mortality from 15 to 25 per cent. For the average physician making a diagnosis of typhus fever is as responsible a task as diagnosing bubonic plague, cholera, etc. Because of this impression which the student carries with him in after years, and with which the general practitioner is imbued, it has been difficult to impress the fact that a variety of that disease is more or less endemic in many parts of this country.

It is with the idea in mind to emphasize the endemic form of typhus fever (Brill's disease), at least from a clinical point of view, that this series of cases is presented.

This series consists of 138 cases, the first case occurring in October, 1913, the last in August, 1927, and comprises those reported from all the medical services of the hospital. The cases were distributed as follows:

	Cases.		Cases.		Cases.
1913 (3 mos.)	4	1918	7	1923	8
1914	22	1919	3	1924	6
1915	22	1920	8	1925	3
1916	19	1921	8	1926	3
1917	11	1922	11	1927	3

Though all these cases were hospital admissions, investigation never revealed more than 1 case either in a family or in a house, and no case could be traced as secondary to exposure. In the absence of any special precautions, no case developed in the hospital either among the patients or the medical and nursing staff.

Etiology.—The specific etiology of typhus began to take form when Plotz in 1915 announced the discovery of his bacillus (Bacillus typhi exanthematici). While his bacillus is now considered only a secondary invader, it stimulated research, and in 1916 daRocha-Lima and Prowazeki reported observations that lice infected with typhus showed countless numbers of microscopic bacillary bodies in the cells lining their stomachs. These bodies were readily recognized as identical with those found by Ricketts in cases of typhus occurring in Mexico. Thus the name of Rickettsia-Prowazeki is given to these bodies. These have not been definitely identified as either protozoan or bacterial in nature. But that at least the body louse is the agent for their transmission has been definitely established by human and animal experimentation.

In our series of cases no very special effort was made to detect lice in patients; a somewhat closer observation than usual revealed these patients to be no more infested than patients suffering from other diseases. This and similar observations made by others make it appear quite improbable that the mode of transmission of the etiological factor by the body louse is the same in endemic typhus as has been proved to exist in epidemic typhus. As Maxcy puts it, "the disease was not associated with lousiness," and suggests the explanation that, at least in the southeastern part of the United States, a reservoir of the disease may exist other than in man, "a rodent reservoir with accidental transmission to man through the bite of some parasite, blood-sucking insect, or arachnid." Whatever the explanation might be, we are convinced that the louse per se is not the direct infective agent in endemic typhus.

Pathology.—Deaths from typhus fever (epidemic) are remarkable for the absence of any characteristic gross pathology;

the lesions encountered being those resulting from any acute infectious disease, such as cloudy swelling of parenchymatous organs, and frequently patches of bronchopneumonia. It was in 1914 that Fraenkel described the distinctive pathology observed microscopically. It is limited to lesions of the blood-vessels, chiefly of the skin and central nervous system. Briefly stated they are as follows: "The focal lesions are found in minute arterioles and capillaries, and consist of marked swelling and proliferation of the lining endothelium, perivascular round-cell infiltration, and a tendency to obliteration of the lumen by hyaline (blood-platelet) thrombi." So pathognomonic of the disease are these lesions that in doubtful cases a biopsy is recommended to establish the diagnosis. This localization of the microscopic pathology explains the two characteristic clinical phenomena, the skin rash and the nervous symptoms. From a pathologic point of view there is never any confusion between typhus and typhoid fever, for in typhoid the gross lesion in the intestinal tract is characteristic, in typhus the intestinal tract is uniformly free from any such lesion. The above description is observed in both types of the disease, the difference noted being one of degree, severe in one, mild in the other.

Before presenting a statistical study of the clinical features of this disease, a brief summary of the symptomatology of endemic typhus will be an appropriate introduction: It is an acute infectious disease, frequently preceded by a short prodromal period followed by a chill or chills, a definite rise in temperature, a severe headache, at times nausea and vomiting, general body pains, an eruption appearing about the fifth day, and characterized during its course by nervous symptoms of various intensity and marked asthenia, terminating in from ten to fourteen days, usually by crisis or rapid lysis.

A statistical study of the clinical features of 138 cases furnish certain data as follows:

Nationality and Race.—All were Hebrews; 95 per cent. of the patients were Russian Hebrews. The remaining 6 were distributed as follows: Austrian 2, German 1, French 1, Roumanian 1, Native American 1. This proportion of Russian

Hebrews is far in excess of the general admissions to the hospital which figure 70 per cent. the maximum, and can be mentioned as a feature of the endemic form of the disease as encountered by us. However, that the Russian Hebrew is not peculiarly susceptible to the disease is demonstrated by Maxcy who found all his cases in the southeastern states, with one or two possible exceptions, native white Americans. Negroes, he reports, enjoy almost complete immunity from the disease.

Season.—Half of the cases (69) occurred during the period between June and October. The other half were seen during the remaining eight months. This is in striking contrast to what occurs in epidemic typhus where the seasonal incidence is winter and early spring, when crowding, poor ventilation, and other unsanitary conditions tend to favor the presence of the body louse.

Sex.—The disease occurred somewhat more frequently in the female, 55 per cent., as compared with the male, 45 per cent.

Age.—The average age was slightly over thirty-nine years, the extremes being fourteen years the youngest, and seventy-two years the oldest.

Period of Incubation.—This has been impossible to determine in any of our cases, since in no single instance was a history of exposure obtained. It has been definitely determined, experimentally and otherwise, to be on the average from eight to twelve days.

Mode of Onset.—This is stated as generally abrupt and only occasionally is a prodromal period observed. Our experience is somewhat at variance with these figures, for only in 76, or 58 per cent., of the cases was the onset abrupt and in 55, or 42 per cent., the onset was preceded by a prodromal period of from two to four days in which general malaise, muscle pains, loss of appetite, etc., occurred, following which the definite symptomatology of the disease was ushered in. This is usually abrupt, beginning with a chill or chills, a marked rise in temperature (102° to 103° F.), a severe headache, nausea, occasionally vomiting, and general body pains. This picture is not unlike that presented by many of the acute infectious diseases. The one

distinguishing feature which is more constant than any other is the headache. This occurs early, usually following the chill, is intense, diffuse, and yields to neither drug nor topical application. Not infrequently a mild photophobia is associated with it. Slight rigidity of the neck is not uncommonly observed. While a definite diagnosis cannot be made the first few days from any combination of symptoms occurring at that time, suspicion of the true nature of the disease is aroused by the severe persistent headache overshadowing the other features of the clinical picture.

The Eruption.—A study of the eruption in this disease must necessarily be incomplete. The disease, as a rule, not being suspected by the general practitioner, an eruption is not looked for. The eruption unless sought for is of such a nature that it is often overlooked, especially if seen by imperfect or artificial light. By the time the patient enters the hospital, which is usually after the disease has lasted for seven days or more, the eruption in endemic typhus is fading and not infrequently has disappeared as a recognizable rash. As a result, our statistics with reference to the beginning of the eruption cover only 20 cases. The eruption began in 5 cases on the fourth day, in 5 on the fifth day, 5 on the sixth day, 4 on the seventh day, and in 1 on the tenth day. The statement, therefore, that 95 per cent. of the patients show an eruption from the fourth to the seventh day, inclusive, is confirmed by the observations generally of those who have had the opportunity of seeing a large number of cases. Its character is not easy to describe, though when once seen it is simple enough. Perhaps the description which best suits it is a "dirty pink color," maculopapular in character, not infrequently measly in outline, appearing on the anterior aspect of the chest near the axillæ, and extending over the shoulders and down the arm a short distance. It is also noticed on the abdomen and occasionally on the back. The eruption bears no resemblance to the roseola of typhoid fever; it differs in many respects. It never appears in crops, it seldom entirely disappears on pressure, showing it to be more than a simple hyperemia (erythema). If we recall the pathology of the disease, we know that besides the local hyperemia some diaped-

esis has taken place; this results in a permanent stain in the skin, characteristic of purpuric rashes.

The eruption in typhus fever is of special importance and significance; important because while typhoid might be diagnosed in the absence of an eruption, typhus could not; its specific pathology is located in the skin, and bears the same relation to the disease as the specific pathology in the intestines bears to typhoid. Significant, because the intensity of the eruption is an index of the severity of the infection and reflects the degree of involvement of the tissues of the central nervous system.

The Temperature.—Fairly constant in type. It begins somewhat abruptly, reaching its fastigium of 103° to 104.5° F. about the third or fourth day, continues with but slight variations till between the tenth and fourteenth day, and then terminates either by crisis or rapid lysis. The average duration of the temperature in our series of cases was approximately twelve days (11.9).

Defervescence.—Crisis was the method of termination of 80, or 60 per cent., of the cases; and 53, or 40 per cent., terminated by lysis, rapid and otherwise. Crisis and lysis are arbitrary terms. When a temperature dropped from nearly its fastigium to normal within twenty-four hours, that was considered a drop of temperature by crisis. When thirty-six or forty-eight hours elapsed, then the drop in temperature was considered as rapid lysis.

The Spleen.—This was definitely palpable in 38, or 28 per cent., of the cases; in 98, or 72 per cent., the spleen was not palpable. Two cases remained doubtful.

Laboratory Data.—The blood-cultures were uniformly negative. The white blood-count averaged 10,750, with 5000 the lowest and 18,000 the highest count. The polymorphonuclear count averaged 73 per cent., the extremes represented by 52 and 90 per cent. The Weil-Felix was begun in 1920 and performed in 45 cases with only two positive and two doubtful reactions and in 40 cases it remained negative. The Weil-Felix reaction in endemic typhus must not be viewed in the same light as the Widal reaction is in typhoid. It should be accepted only as

confirmatory evidence, and not diagnostic in the absence of the characteristic picture of the disease. In the endemic type of typhus, Brill states that his experience with this reaction is disappointing, for the serum seldom gives the reaction in dilutions sufficiently high to be of diagnostic value. Experience in this regard varies, and yet, as stated before, a positive Weil-Felix in the absence of characteristic clinical phenomena is not conclusive.

Complications.—Endemic typhus with its almost negligible mortality nevertheless is associated with complications, at times of a severe nature. In our series they occurred as follows:

Bronchopneumonia	4
Bronchopneumonia with cerebral embolus	1
Pleurisy with effusion, pneumonia, and phlebitis	1
Pneumonia–myocarditis–toxic encephalitis	1
Acute mania	1
Myositis	1
Intercostal neuralgia	1
Femoral thrombophlebitis with pulmonary embolism	1
Suppurative parotitis	2
Otitis media and diabetes	1
Cholecystitis	1
Pulmonary tuberculosis (?)	1
Acute tonsillitis	1
Deltoid bursitis	1

Prognosis.—In spite of the formidable nature of some of these complications, recovery followed in all but two instances. The variation in frequency with which complications are met in this form of the disease is well shown by the report in Maxcy's series of 114 cases, in which only 4 showed complications, in contrast to 18 in this series of 138 cases. In the main the complications in the endemic form resemble those reported as occurring in the epidemic variety. Gangrene was not met with in any case.

A brief account of the last case observed shows some of the characteristics of the disease.

Case: Hospital No. 108,151.—E. B., female, aged fifty-six, Austrian, housewife, admitted August 24, 1927, complaining of

severe headache, backache, chills and fever for six days' duration. One day before admission (the fifth day) a rash was noted on the body. Her past history was irrelevant.

The Present Illness.—This dates back to six days ago when, after not feeling just right for a day or two, she was suddenly seized with a severe chill and headache. The headache persisted, and the patient experienced additional chilly sensations. A physician was summoned, and a diagnosis of grippe was made. Soon after the onset a slight cough developed. On the day before admission (the fifth day) an eruption on the body was noticed.

Physical Examination.—An obese female of fifty-six years, face flushed, lips cyanotic, respiration rapid, appearing acutely ill. Over the bases of both lungs numerous fine crepitant râles were heard, with exaggerated breath-sounds over the same areas. Over the upper chest, the abdomen, the flexor services of both arms was observed a diffuse maculopapular eruption of a "dirty pinkish" color, irregular in size (3 to 6 mm.), and disappearing only partially on pressure. The spleen was at no time palpable. There was no neck rigidity.

Course of the Disease.—Patient appeared toxic and drowsy on admission; headache persisted and was quite intense. A spinal tap gave but little relief; the cerebrospinal fluid flowed under moderately increased pressure. Four days after admission the temperature fell abruptly from 104.6° to 99.4° F.; marked clinical improvement resulted. The patient was brighter, the headache was gone, and the eruption faded. The drop in temperature lasted less than twenty-four hours, and rapidly rose to 103.2° F.; remained elevated for three days; during this febrile period the symptoms returned.

Two days after her admission a few pediculi were seen on the body, and many ova were found attached to the hair. The signs in the chest persisted, and the temperature began to drop on the thirteenth day, reaching normal on the fourteenth. During the course of the disease the pulse ranged from 80 to 112, never dichrotic. Following the drop in temperature marked asthenia was present, with a few scattered residual râles at both bases.

Laboratory Data.—The urine was negative; the white blood-cells, 9600 to 11,800; polymorphonuclears, 72 to 75 per cent.; red blood-cells 3,800,000, with 80 per cent. hemoglobin. The blood-pressure was 94/54, 114/74. The blood-culture was sterile, the Wassermann negative, the Widal and Weil-Felix also repeatedly negative. The spinal fluid showed no bacteria; cytology, 6 lymphocytes per c.mm.; albumin, 1 mm. ring, Fehling's reduced, and globulin negative. The patient was discharged September 14, 1927. A stay in the hospital of twenty-one days.

Differential Diagnosis.—The first essential in the diagnosis of this disease is to remember that it exists, and that it is met with in various parts of the country. At times it must be differentiated from influenza, pneumonia, meningitis, endocarditis, purpura, acute leukemia, and typhoid fever. Of all these diseases the most difficult differential diagnosis is between it and influenza, especially in the presence of some respiratory complication. The absence of upper respiratory infection, the steadier temperature, the leukocytosis and polynucleosis, the abrupt termination, the presence usually of the persistent and unyielding headache, the characteristic rash at about the fifth or sixth day, all these should be sufficient to establish with some degree of certainty the diagnosis. In considering the other conditions which at times cause confusion, the element of time will be of great help. Typhoid fever should seldom present any difficulty. Only because it is customary to suspect typhoid, when a fever continuing for four or five days remains undiagnosed, does the question of differentiation ever arise. The abrupt onset, the temperature reaching its fastigium so early, the severe headache, the rapid pulse, the absence of a leukopenia and relative lymphocytosis, the negative blood-culture, and the character of the rash, all aid in making the differential diagnosis between endemic typhus and typhoid fever early and decisively.

Treatment.—In the absence of a specific, the treatment is symptomatic with special attention to the hygiene of the mouth, the giving of sufficient amounts of liquid, the ice-cap to the head, an occasional dose of acetphenetidin and caffein; if necessary to control the restlessness and headache, codein or morphin

may be given. If the headache is associated with rigidity of the neck, lumbar puncture might give relief. Digitalis in failing circulation is indicated. Convalescence is often prolonged; it should never be hastened.

There are two other medical services in the hospital. I included in this summary some (though only a few) of their cases. I wish to thank them.